The Archives of Internal Medicine

Vol. XIV SEPTEMBER, 1914 No. 3

INTRODUCTION TO THE SECOND PROGRESS REPORT OF THE THOMPSON-McFADDEN PELLAGRA COMMISSION *

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The investigations of the Thompson-McFadden Pellagra Commission have been directed especially toward the study of the etiological factors in pellagra. We conceive this problem to include not only a study of the nature of the disease, the recognition and identification of the essential infecting or intoxicating agent, or the recognition of the dietary elements, the deficiency of which may give rise to pellagra, but also necessarily a study of the disease in its endemic centers, a study of the people who live there, their habits of life, their environment and occupations and their food, and, especially, a careful scrutiny of those respects in which the non-pellagrins of such a population differ from the pellagrins living in the same regions.

During the course of this work we have undertaken to record every known case of pellagra existing within a limited geographical district,[1] namely, Spartanburg County, S. C., to examine personally each suspected case, and to record a detailed history of each pellagrin in whom a reliable diagnosis could be made. The records actually made in respect to each case are quite elaborate and include a complete history of the individual from birth, with particular attention to foods, occupations, residences, relationships and diseases, as well as a careful description of the present environment and life of the individual. By the aid of maps of Spartanburg County, and larger more detailed maps

* Submitted for publication, March 20, 1914.

* From the Division of Tropical Medicine, Department of the Laboratories, New York Post-Graduate Medical School and Hospital.

* Read in part before Section K, American Association for the Advancement of Science, Atlanta, Ga., Jan. 2, 1914.

1. The general plan of the epidemiological studies in 1912 has been outlined in detail in Section II of the First Progress Report. See Siler and Garrison: Am. Jour. Med. Sc., 1913, cxlvi, 42.

of the more thickly populated districts, each known case of pellagra has been located, and the houses known to have been occupied at any time by a pellagrin have been designated.

In intimate collaboration with this commission, the Bureau of Entomology of the United States Department of Agriculture has undertaken a comprehensive study of the insects which occur in the region studied, with special attention to their possible relationship to pellagra. This work included a general entomological survey of the territory, an examination of all insects found there in association with man, and a particular study of those species the biology of which suggested a possible relation to the spread of pellagra.

Detailed clinical and pathological studies were carried out on selected patients. Fourteen of these patients were transferred to the Post-Graduate Hospital in New York and treated there during the continuance of the active manifestations of the disease. During their residence in the hospital a careful study of their metabolism in general and, in particular, of the utilization of foods, was carried out. For hematological studies, blood was obtained from these patients and also from pellagrins at their homes in the South. The hospital cases also furnished an important part of the material for study of intestinal micro-organisms and for experimental inoculation of animals, although other cases have also been utilized in this work. Finally, these cases were the objects of a clinical study, and their hospital records present information concerning the course of the attack of pellagra when it is uninfluenced by attempts at specific medication.

Certain progress reports on the investigations of the commission in 1912 were presented at the National Pellagra Conference at Columbia, S. C., in October of that year, and these reports have been published in succeeding numbers of the *American Journal of the Medical Sciences*[2] from March to August, 1913. A summary of these reports was presented at the Pellagra Meeting in Spartanburg, S. C., Sept. 5, 1913 and appeared in the *Journal of the American Medical Association*,[3] Jan. 3, 1914. These papers have since been brought together and issued as the First Progress Report of the Thompson-McFadden Pellagra Commission.

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2. Hillman, O. S.: Some Hematological Findings in Pellagra, Am. Jour. Med. Sc., 1913, cxlv, 507. Myers, V. C., and Fine, M. S.: Metabolism in Pellagra, ibid., 1913, cxlv, 705. MacNeal, W. J.: Observations on the Intestinal Bacteria in Pellagra, ibid., 1913, cxlv, 801. Siler, J. F., and Garrison, P. E.: An Intensive Study of the Epidemiology of Pellagra, Report of Progress, ibid., 1913, cxlvi, 42, 238. Jennings, A. H., and King, W. V.: An intensive Study of Insects as a Possible Etiologic Factor in Pellagra, ibid., 1913, clxvi, 411.

3. Siler, J. F., Garrison, P. E., and MacNeal, W. J.: Pellagra: A Summary of the First Progress Report of the Thompson-McFadden Pellagra Commission, Jour. Am. Med. Assn., 1914, lxii, 8.

A considerable part of the work done in 1912 has not been included in these published reports for various reasons, but chiefly because of incompleteness of the work. This applies especially to the attempts to produce pellagra in animals by experimental inoculation, the clinical observations on the pellagrous patients treated in the hospital and the pathological study of necropsy material.

The work done in 1913 has been directly continuous with that of 1912, and supplements and extends the observations of that year. Our main efforts have been devoted to the epidemiologic studies, chiefly because these studies were expected to indicate the fruitful fields for other experimental investigations. The method of epidemiologic study has been continued along the same lines as before, and has been further developed in two special directions; first, we have endeavored to obtain more complete information concerning every person living in certain selected industrial and rural communities in which pellagra is prevalent; and second, we have extended our field of observation to cover other selected communities resembling these in many respects, but showing marked differences in certain particulars, as, for example, in the prevalence of pellagra; the presence or absence of certain insects; the possession of a topography which would necessitate a difference in insect fauna, in the density of population, or in the method of disposal of human wastes.

Inasmuch as the work of 1912 had shown an especially high prevalence of pellagra in the cotton-mill villages, several of these were selected for intensive detailed study, and one rural district in which many cases of pellagra had occurred was studied in a similar way. The communities selected for observation because they exhibited special features could not be examined in such detail, as in many instances they were situated at a distance from our working base. For this study we selected certain mill villages situated in Oconee, Chester and Union counties in South Carolina; a rural district in Georgetown County, on the coast of South Carolina; a large island off the coast near Charleston, S. C., and a portion of the arid region of Texas. At the courteous invitation of Dr. L. W. Sambon, we were enabled to extend these observations to the British West Indies.

The metabolism studies of 1912 had yielded definite negative information and seemed to be sufficiently complete and were therefore discontinued. The study of the blood has been continued and a further report will be forthcoming. Further observations on the intestinal micro-organisms have been made and the attempts to produce pellagra in animals have been zealously pushed. The clinical observations have been continued in cases of pellagra treated in a hospital in Spartanburg, S. C.

The cooperation of the Bureau of Entomology of the United States Department of Agriculture has continued during the past year. The

work undertaken by this bureau has included a particularly careful study of insects in the endemic foci of pellagra and carefully controlled attempts at the experimental transmission of pellagra by means of certain of these insects.

We desire to make special acknowledgment to Dr. L. O. Howard, chief of the Bureau of Entomology, and to the field workers of the bureau, Mr. A. H. Jennings, Mr. W. V. King and Mr. A. W. J. Pomeroy, for this cooperation.

We are indebted to the American Genetic Association for the cooperation of its representative, Dr. Elizabeth Muncey, who has made a study of heredity in pellagra; to the Board of Administration of the state of Illinois for the collaboration of Dr. H. Douglas Singer, who spent several weeks with us studying the early nervous and mental manifestations of pellagra; to Dr. J. W. Babcock of Columbia, S. C., for generous assistance and valuable material; to Dr. E. M. Green, clinical director of the Georgia State Sanitarium, Milledgeville, Ga., and to members of his staff for similar cooperation; to Dr. J. A. Hayne, secretary of the South Carolina State Board of Health, for much valuable information and assistance; to Dr. L. W. Sambon of London, and to the government officials of Jamaica, Panama, Barbados and Trinidad, for courteous assistance and extensive records relating to pellagra.

Our field laboratory has been visited during 1913 by a number of noted scientists and students of pellagra; among them Dr. J. W. Babcock of the South Carolina State Hospital, Columbia, S. C.; Surg.-Gen. Rupert Blue of the United States Public Health Service, Washington, D. C.; P. A. Surg. R. M. Grimm of the United States Public Health Service; Dr. W. D. Hunter of the Bureau of Entomology, United States Department of Agriculture; Mr. M. E. MacGregor of Cambridge University, Cambridge, England; Mr. Paul Marchal of the French Department of Agriculture, Paris; Mr. C. W. Mason of Cambridge University, Cambridge, England; Dr. George N. Miller of the New York Post-Graduate Medical School and Hospital, New York; Drs. G. M. Niles, S. R. Roberts and G. C. Mizell of Atlanta, Ga.; Dr. L. W. Sambon of the London School of Tropical Medicine, London; and Dr. E. J. Wood of Wilmington, N. C. We are grateful to these men for their encouragement and counsel.

We desire to make special acknowledgment to Dr. Paul A. Schule, whose addition to the staff of the commission has contributed much to the success of the year's work.

It is our purpose to present, as the Second Progress Report of this commission, a series of papers by the various investigators, dealing with several phases of the work of the year 1913.

Twentieth Street and Second Avenue.

A STATISTICAL STUDY OF THE RELATION OF PELLAGRA TO USE OF CERTAIN FOODS AND TO LOCATION OF DOMICILE IN SIX SELECTED INDUSTRIAL COMMUNITIES *

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Our most intensive epidemiologic studies have been carried out in six cotton-mill villages in Spartanburg County, S. C., selected as fairly representative of the many mill villages in that part of the country. In each of these villages the family of each operative was visited at his home and a complete record was taken on a uniform printed card, of the location of the house, the sex, age, relationship, occupation, period of present residence and association with pellagra, of each inhabitant. On the reverse side of the same card was recorded the frequency of use of certain important elements of the diet and the condition of the house in respect to screening and general condition.

Whenever a case of pellagra was found, the usual complete history of the individual was taken, and this included a record of the previous residences of the individual, the time of the first attack and a very complete record of his diet. These records make possible statistical studies of the distribution of pellagra in these populations to ascertain its correlation with various other things, as, for example, age, sex, occupation, use of particular foods, location of the domicile or sanitary condition of the home. They seem to us to be of peculiar value for the study of the influence of foods on pellagra and for an inquiry as to the possible bearing which location of domicile may have in the causation of this disease. In the present paper we purpose to present, first, a study of the relation of pellagra to certain foods, and second, a study of the relation between the domicile of existing cases of pellagra and the domicile of the new cases which originated in

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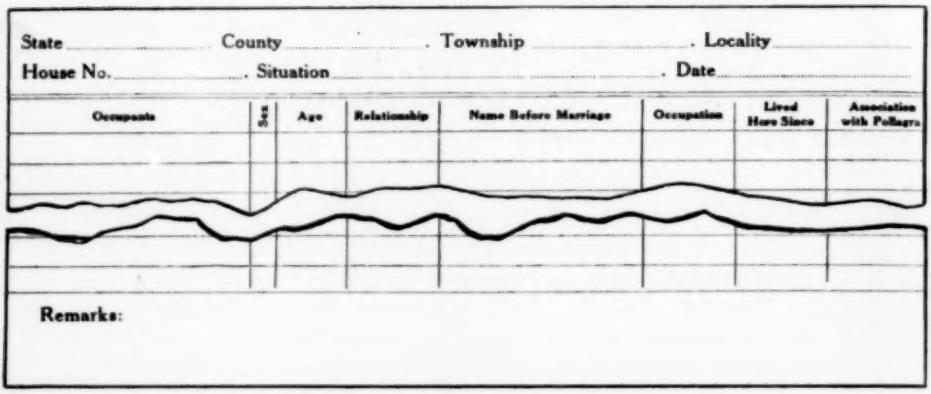
these villages. The two studies have been carried out by much the same method, and because of their interrelationships and the sharp contrast in their results, it has been thought best to present them in a single contribution.

THE RELATION OF PELLAGRA TO THE USE OF PARTICULAR FOODS

In view of the apparent importance of nutrition as an etiological factor in pellagra, and because of the confident belief of many authorities that the disease is due to deficiency in diet, either general or special, or that it is a specific food intoxication, we have undertaken a careful investigation of the dietary habits, not only of pellagrins and their families, but also of all the remaining population of the same class living under the same conditions, in certain selected


State ..... County ..... Township ..... Locality .....
House No. ..... Situation ..... Date .....

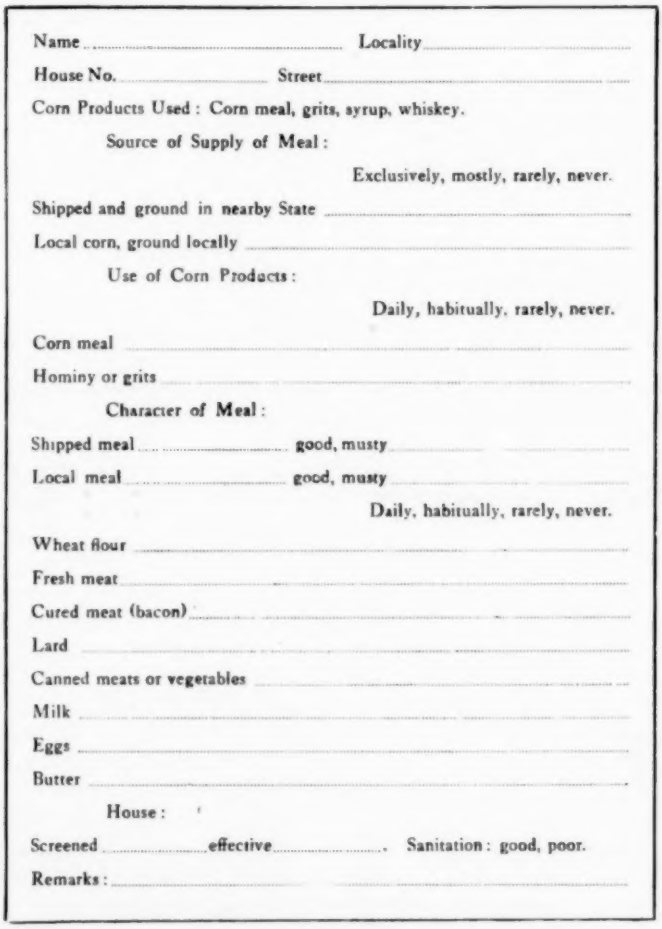
Occupants	Sex	Age	Relationship	Name Before Marriage	Occupation	Lived Here Since	Association with Pellagra

Remarks:

Fig. 1.—Census card used in the house-to-house canvas.

industrial communities. Approximately five thousand persons have been included in these studies. The facts were ascertained for each family by personal interview with a member of the family, usually the housewife. We recorded the diet served in the family as a whole, and each member of the household is considered as belonging to the dietary group of his family. For each pellagrin, the individual diet was recorded in detail, but for the comparative study which we present in this section, each of these persons is considered as belonging to the dietary group of his family, not only because this makes them strictly comparable to the other individuals, but also because the individual peculiarities in the diet of pellagrins, particularly the omission of corn from the diet, may often be regarded as secondary to the development of the disease.

In obtaining the data a uniform printed card was used and the record was made concerning the frequency of the use of shipped corn-meal, locally grown corn-meal, and the quality of the meal used; concerning the use of grits, corn-sirup, corn whisky, wheat flour, fresh


Name ..... Locality .....

House No. ..... Street .....

Corn Products Used: Corn meal, grits, syrup, whiskey.

Source of Supply of Meal:

Exclusively, mostly, rarely, never.

Shipped and ground in nearby State .....

Local corn, ground locally .....

Use of Corn Products:

Daily, habitually, rarely, never.

Corn meal .....

Hominy or grits .....

Character of Meal:

Shipped meal ..... good, musty .....

Local meal ..... good, musty .....

Daily, habitually, rarely, never.

Wheat flour .....

Fresh meat .....

Cured meat (bacon) .....

Lard .....

Canned meats or vegetables .....

Milk .....

Eggs .....

Butter .....

House:

Screened ..... effective ..... Sanitation: good, poor.

Remarks: .....

Fig. 2.—Reverse side of the census card.

meats, cured meats, canned meats, vegetables and fruits (tinned foods), and concerning leaf-lard, compound lard, vegetable oils, milk, butter and eggs. In respect to the frequency of use, we recognized seven classes: first, daily use which is self-explanatory; second, habitual use,

meaning as often as twice a week on the average; third, part time daily, which means daily use during certain seasons of the year; fourth, part time habitually, or habitual use during certain seasons; fifth, rarely, which means use less frequently than twice a week; sixth, part time rarely; and seventh, never.

DIETARY ELEMENTS DISMISSED FROM CONSIDERATION

Certain of these articles were not very commonly used and there is evidently no important reason for giving them detailed consideration. This applies particularly to corn-grits and corn-sirup. Corn whisky was not used by many, possibly in part because of legal restriction of the liquor traffic in the territory studied. For the most part, it was used only by the adult males, a class of the population in which pellagra was not very prevalent. It has not, therefore, seemed worth while to assemble and analyze the data in regard to it. Wheat flour was used daily by every family in the population studied. No distinction between pellagrins and non-pellagrins could be ascertained in respect to this dietary element. The recorded data in respect to lard are difficult to analyze because so many different brands were used and we have not, as yet, obtained reliable information concerning their composition. The remaining foods concerning which information has been gathered, namely, shipped corn-meal, local corn-meal, fresh meat, canned (tinned) foods, milk and eggs will be considered.

METHOD OF PRESENTATION

The general method of analyzing these data consists in dividing the population into several groups, distinguished from each other by the frequency with which the particular food was used, and then comparing the relative number of cases of pellagra in the different groups. Four distinct possibilities present themselves. We may consider as a unit each family present in the village at the time of our census, and compare the families in which pellagra existed with the total families present, or we may consider each individual in the same population as a unit and compare the total existing pellagrins with the total population. These two analyses might be expected to agree with each other fairly well, and should indicate the possible relation of diet to the presence of pellagra, both new and recurrent cases being considered together. Third, we may consider as a unit each family of which we have record, which lived in the particular village in 1912 or 1913 and compare the families in which *new cases* of pellagra appeared, with the total families, and fourth, we may examine the same population in a similar way, considering each individual person as a unit. The last two analyses might be expected to agree with each

other and should reveal the relation of these dietary constituents to new cases of pellagra. The latter would probably be a more accurate indication of the importance of the particular foods as predisposing factors, or as vehicles of the directly active etiological agents. Because of the manifest importance of this dietary phase of the subject of pellagra, we have undertaken to study our data in all four of the ways mentioned.

SHIPPED CORN-MEAL

The records in regard to the use of shipped corn include 853 families, present in the six villages in the year 1913, in 137 of which one or more pellagrins existed at the time. The distribution of these 853 families in respect to the frequency of use of shipped corn-meal is indicated in Table 1.

TABLE 1.—DISTRIBUTION OF TOTAL FAMILIES ACCORDING TO FREQUENCY OF USE OF SHIPPED CORN-MEAL

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	47	14	8	11	5	2	15	102
W	44	18	4	16	2	0	11	95
P	116	51	22	12	2	1	18	222
Sa	38	15	10	10	6	3	19	101
A	33	22	14	6	1	2	4	82
Sp	130	40	27	14	8	1	31	251
Total..	408	160	85	69	24	9	98	853

It will be noted that this foodstuff was a staple article of diet, used daily by nearly half the families and never used by only about 11 per cent. of them. There was evidently not much difference between the various villages in the use of this food. At the larger mills, P and Sp, more than half the families used it daily, while in one village, Sa, only 38 of 101 families did so. The other villages are intermediate in this respect.

The distribution of the 137 families in which pellagra was present, in respect to frequency of use of shipped corn-meal, is indicated in Table 2.

By grouping together those families using shipped corn-meal habitually, part time daily and part time habitually under the heading, *Habitually,* and the groups using it rarely, part time rarely and never, together under the heading *Rarely,* Tables 3 and 4 are obtained.

TABLE 2.—Families Containing One or More Cases of Pellagra Distributed According to Frequency of Use of Shipped Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	5	3	1	2	0	0	2	13
W	10	6	1	1	0	0	1	19
P	10	9	5	2	0	0	2	28
Sa	11	4	2	3	1	2	6	29
A	7	5	4	0	0	0	1	17
Sp	13	6	2	5	1	1	3	31
Total..	56	33	15	13	2	3	15	137

TABLE 3.—Summarized Distribution of Families According to Frequency of Use of Shipped Corn-Meal

Village	Total Families			Pellagrin Families		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	47	30	25	5	5	3
W	44	36	15	10	7	2
P	116	65	41	10	11	7
Sa	38	31	32	11	8	10
A	33	29	20	7	5	5
Sp	130	62	59	13	12	6
Total	408	253	192	56	48	33

TABLE 4.—Pellagrin Families in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	10.6	16.7	12.0	12.7
W	22.7	19.4	13.3	20.0
P	8.6	16.9	17.1	12.6
Sa	28.9	25.8	31.3	28.7
A	21.2	17.2	25.0	20.7
Sp	10.0	19.4	10.2	12.4
Total.....	13.7	19.0	17.2	16.1

The large villages, Sp and P, show relatively fewer families with cases of pellagra, while in the village Sa, in which shipped corn-meal was less frequently used, nearly 29 per cent. of the families contained one or more cases. In three of the villages, P, Sa and A, the families using shipped meal rarely or never were most frequently afflicted with pellagra. In only one village, W, is the percentage of pellagrin families highest in the group using this food daily, and for the total families of the six villages this group shows relatively the least pellagra. The figures are rather irregular and inconsistent, but on the whole they seem to us to indicate that families containing one or more pellagrins tend in some instances to restrict their use of shipped corn-meal. The tables do not reveal any positive correlation between the use of this food and the occurrence of pellagra.

The 853 families just considered included 5,151 persons, among whom 196 were pellagrins. The distribution of these 5,151 persons in respect to the frequency of use of shipped corn-meal is shown in Table 5.

TABLE 5.—Distribution of Total Individuals According to Frequency of Use of Shipped Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	286	75	38	71	40	13	65	588
W	275	92	20	90	14	0	74	565
P	737	331	121	74	16	5	82	1,366
Sa	244	101	49	63	35	20	123	635
A	171	138	102	81	3	7	23	525
Sp	800	225	151	88	44	4	160	1,472
Total..	2,513	962	481	467	152	49	527	5,151

On the whole, approximately half these persons were members of families in which shipped corn-meal was used daily. In the large villages, P and Sp, more than half the persons were members of such families, while in the village A, less than one-third of the population took this food daily, and in Sa, considerably less than half. The distribution of the 196 pellagrins in this population in respect to the frequency of use of shipped corn-meal is given in Table 6.

A consideration of the pellagra morbidity in each village for each of the seven degrees of frequency in the use of shipped corn-meal is omitted because of the small size of certain of the groups. By assembling the figures into groups representing three degrees of frequency, namely, daily, *habitually* and *rarely* (including never) it is possible to obtain groups of some size (Tables 7 and 8).

TABLE 6.—Distribution of Pellagrins According to Frequency of Use of Shipped Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	8	3	1	3	0	0	4	19
W	11	7	3	2	0	0	1	24
P	10	11	8	4	0	0	4	37
Sa	16	4	2	3	2	3	13	43
A	12	7	7	0	0	0	1	27
Sp	19	9	5	6	1	1	5	46
Total..	76	41	26	18	3	4	28	196

TABLE 7.—Summarized Distribution According to Frequency of Use of Shipped Corn-Meal

Village	Total Population			Individual Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	286	186	116	8	6	5
W	275	196	94	11	9	4
P	737	421	208	10	15	12
Sa	244	199	192	16	9	18
A	171	222	132	12	7	8
Sp	800	357	315	19	16	11
Total	2,513	1,581	1,057	76	62	58

TABLE 8.—Pellagra Morbidity in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	2.80	3.22	4.31	3.23
W	4.00	4.59	4.26	4.25
P	1.36	3.56	5.77	2.71
Sa	6.56	4.52	9.37	6.77
A	7.02	3.15	6.06	5.14
Sp	2.38	4.48	3.49	3.13
Total.....	3.02	3.92	5.49	3.81

The comparative study of pellagra morbidity in these groups for each of the six villages shows no definite consistent tendency for it to vary with the frequency of use of shipped corn-meal. In three villages, I, P and Sp, and in the total population of the six villages considered together, the pellagra morbidity varies inversely with the frequency of ingestion of this food, that is, those who eat it every day have the least pellagra, and those persons taking it rarely show the greatest morbidity. In the other three villages the relationship is irregular. The total pellagra morbidity in the larger villages, P and Sp, in which shipped corn-meal was most extensively used, is the lowest, namely, 2.71 and 3.13 per cent., respectively, while the greatest relative morbidity is shown by the villages Sa and A, in which shipped corn-meal was least used. This consideration of individuals leads, therefore, to the same general conclusion as did the consideration of the families, namely, that there is slightly more pellagra in those who use shipped corn less frequently. As has been suggested, this may be due to a tendency of some pellagrins to restrict their ingestion of this food. At any rate it is clearly evident that this examination of our recorded data has failed to reveal any close connection between the use of shipped corn-meal and the existence of pellagra in the population of these six mill villages.

In order to ascertain more exactly the probable importance of shipped corn-meal in the causation of pellagra, we have undertaken a study of cases of the disease which originated in these six mill villages during the period of our observations (1912 and 1913). In this study we have included all families residing in the particular village at the time of our census in 1913, and in addition all other families on our records in which cases of pellagra originated in the respective village in 1912 or 1913. The population considered is therefore not exactly the same as that utilized above, but it is very largely identical with it. The records include 865 families, and in 85 of these families one or more cases of pellagra developed in 1912 or 1913.

The distribution of these 865 families according to the frequency of use of shipped corn-meal is indicated in Table 9.

Table 9 is very similar to Table 1, but includes a few more families which had moved away from the respective village after one or more of their members had contracted pellagra there. The distribution of the 85 families in which cases of pellagra originated in 1912 or 1913 in these villages is given in Table 10.

Assembling the families into three groups in respect to frequency of use of shipped corn-meal, the figures in Table 11 are obtained.

There is evidently no consistent relationship between the frequency of the use of shipped corn-meal and the occurrence of new cases of

TABLE 9.—Distribution of Total Families According to Frequency of Use of Shipped Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	49	15	8	11	6	2	15	106
W	45	18	4	16	2	1	12	98
P	116	51	22	12	2	1	18	222
Sa	40	15	10	10	6	3	19	103
A	33	22	14	6	1	3	4	83
Sp	131	40	27	14	8	1	32	253
Total..	414	161	85	69	25	11	100	865

TABLE 10.—Distribution of Families in Which New Cases of Pellagra Occurred in 1912 or 1913, According to Frequency of Use of Shipped Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	7	3	1	2	1	0	2	16
W	6	1	0	1	0	1	2	11
P	8	4	5	1	0	0	1	19
Sa	6	2	0	0	1	2	1	12
A	3	4	2	0	0	1	0	10
Sp	8	3	1	2	0	0	3	17
Total..	38	17	9	6	2	4	9	85

TABLE 11.—Summarized Distribution of Families According to Frequency of Use of Shipped Corn-Meal

Village	Total Families			Families with Incident Pellagra		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	49	32	25	7	6	3
W	45	36	17	6	2	3
P	116	65	41	8	5	6
Sa	40	31	32	6	3	3
A	33	29	21	3	4	3
Sp	131	62	60	8	5	4
Total	414	255	196	38	25	22

pellagra to be seen in these tables. The figures for the six villages combined suggest rather that new cases were slightly more frequent in families using this food product rarely or never. Here also, the lowest incidence of pellagra is in the large villages, P and Sp, the only ones in which shipped corn-meal was used daily by more than half the families.

TABLE 12.—Families with Incident Pellagra in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	14.3	18.8	12.0	15.1
W	13.3	5.6	17.6	11.2
P	6.9	7.7	14.6	8.6
Sa	15.0	9.7	9.4	11.7
A	9.1	13.8	14.3	12.0
Sp	6.1	8.1	6.7	6.7
Total.....	9.2	9.8	11.2	9.8

TABLE 13.—Distribution of Individuals According to Frequency of Use of Shipped Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	300	89	38	71	44	13	65	620
W	272	86	20	89	14	6	77	564
P	736	324	119	72	16	5	79	1,351
Sa	248	99	47	60	34	20	112	620
A	165	135	99	81	3	12	23	518
Sp	794	219	149	84	43	3	165	1,457
Total..	2,515	952	472	457	154	59	521	5,130

The 855 families just considered included 5,130 persons who did not have pellagra at the beginning of the year 1912, so far as we have been able to ascertain. Persons known to have contracted pellagra previous to 1912 have been excluded from this number. Of these 5,130 persons, 110 contracted pellagra during the years 1912 and 1913. The distribution of the 5,130 individuals of this population in respect to the frequency of the use of shipped corn in their families is shown in Table 13.

Table 13 resembles Table 5, but the population considered is not quite the same. Old cases of pellagra existing previous to 1912 are

excluded from this table and some other persons have been included who, although not residing in these villages at the time of our census in 1913, nevertheless did reside there in 1912 or 1913 when some member of their family contracted pellagra. The 110 persons who contracted pellagra in these villages in 1912 and 1913 were distributed according to frequency of use of shipped corn by their families as follows:

TABLE 14.—Distribution of Incident Pellagrins According to Frequency of Shipped Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	10	3	1	3	1	0	4	22
W	6	1	0	1	0	3	2	13
P	9	4	6	2	0	0	1	22
Sa	6	2	0	0	1	3	2	14
A	6	4	4	0	0	1	0	15
Sp	11	3	3	2	0	0	5	24
Total..	48	17	14	8	2	7	14	110

By assembling these figures into the groups representing the three degrees of frequency of use of shipped corn-meal, Tables 15 and 16 are obtained.

It is clearly evident, from these tables, that the occurrence of new cases of pellagra in these mill villages shows no definite consistent tendency to vary with the frequency of use of shipped corn-meal. On the contrary, in every one of these six villages the incidence of the disease actually observed was highest in that portion of the population which rarely or never used this foodstuff. In the total population of the six villages the occurrence of new cases of pellagra was almost twice as frequent in those using shipped meal rarely as in the groups using it daily or habitually. These results lend no support to the conception that pellagra is caused by the ingestion of shipped corn-meal in these particular mill villages and they seem to us to render very insecure the theory that imported or shipped corn may anywhere be regarded as the essential cause of pellagra.

LOCAL CORN-MEAL

The recorded data in regard to the use of local or home-grown corn-meal relate to 866 families present at the time of our ceusus, of which 134 contained one or more cases of pellagra at that time. The distribution of these 866 families in respect to the frequency of use of local corn-meal is given in Table 17.

TABLE 15.—Summarized Distribution According to Frequency of Use of Shipped Corn-Meal

Village	Total Population			Incident Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	300	204	116	10	7	5
W	272	189	103	6	2	5
P	736	412	203	9	6	7
Sa	248	193	179	6	3	5
A	165	219	134	6	4	5
Sp	794	346	317	11	5	8
Total	2,515	1,563	1,052	48	27	35

TABLE 16.—Incidence of Pellagra in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	3.33	3.43	4.31	3.55
W	2.21	1.06	4.85	2.30
P	1.22	1.46	3.45	1.63
Sa	2.42	1.55	2.79	2.26
A	3.64	1.83	3.73	2.90
Sp	1.39	1.44	2.52	1.65
Total.....	1.91	1.73	3.33	2.14

TABLE 17.—Distribution of Total Families According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Dailv	Habitually	Rarelv		
I	5	7	1	11	5	2	72	103
W	8	3	1	16	3	0	77	108
P	8	4	4	12	2	1	192	223
Sa	10	7	2	10	6	3	60	98
A	0	1	4	7	1	2	67	82
Sp	5	3	2	13	7	1	221	252
Total..	36	25	14	69	24	9	689	866

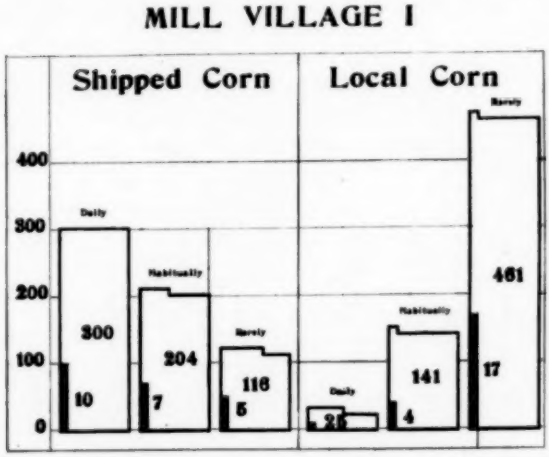


Fig. 3.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

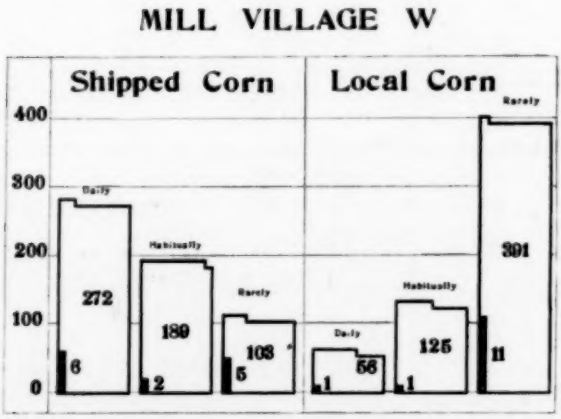


Fig. 4.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

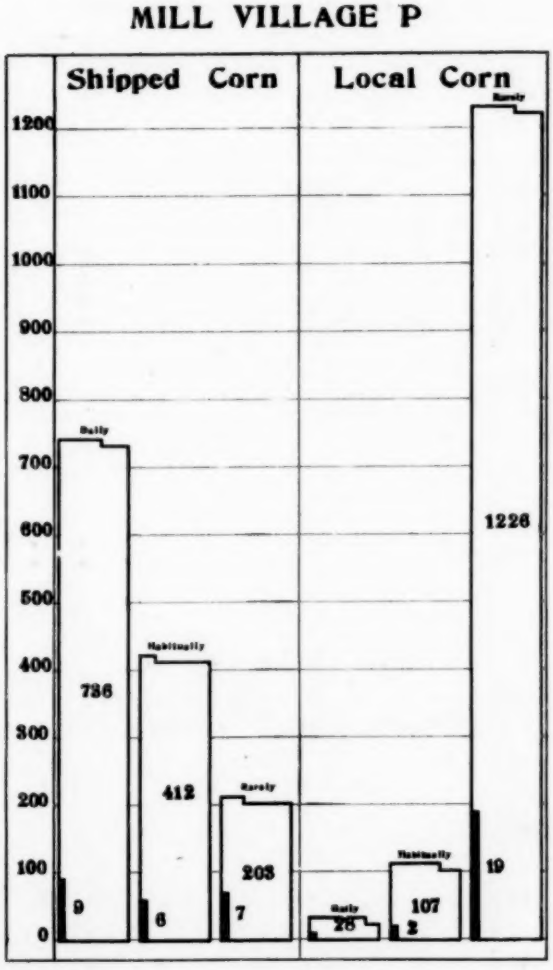


Fig. 5.—The area of each large white column indicates the number of non-pellagrin individauls using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

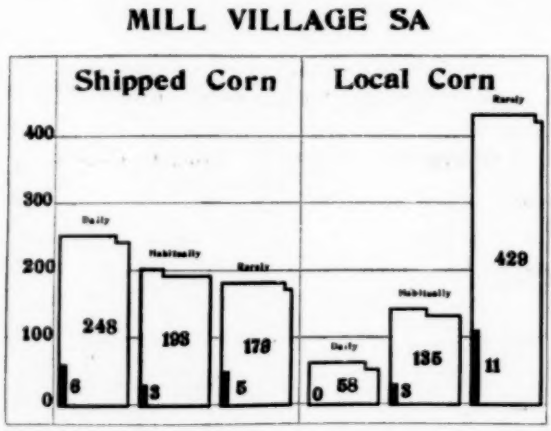


Fig. 6.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

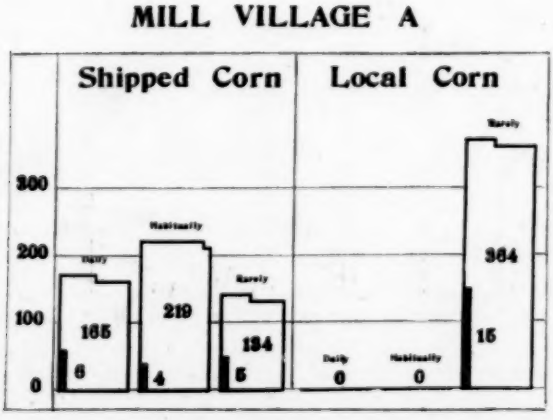


Fig. 7.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

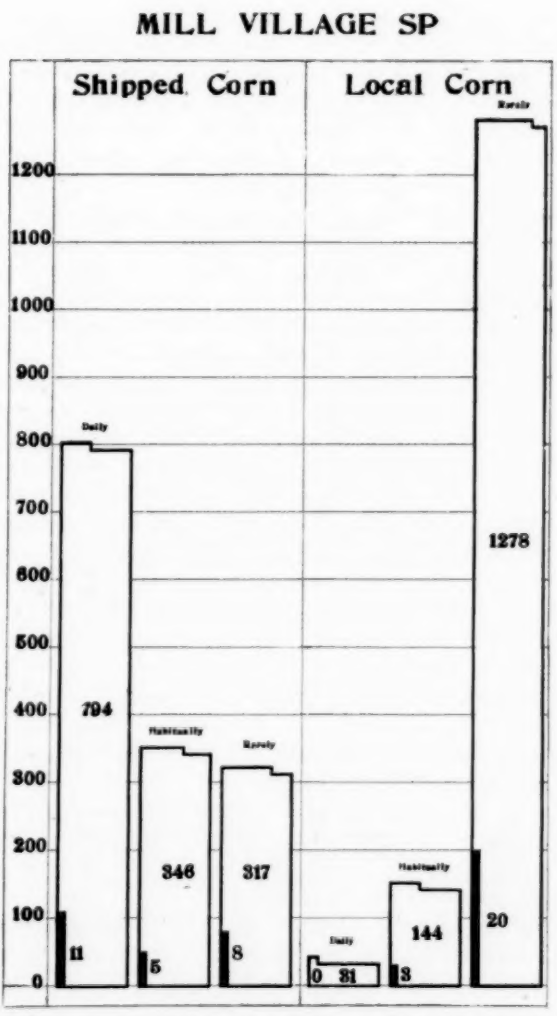


Fig. 8.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

It will be noted at once that local corn was not very extensively used. More than three-quarters of the total families never used it. It was most largely used in the village Sa, and used by relatively least number of families in the large villages of P and Sp. The distribution of the 134 families containing one or more cases of pellagra in respect to the frequency of use of local corn is shown in Table 18.

By assembling these figures into the usual three summarized groups in respect to frequency of use of the food, the figures shown in Table 19 are obtained.

It will be noted that the percentage of families having one or more cases of pellagra was highest in the village Sa, namely, 24.5 per cent., in which, as we have seen above, local corn-meal was most extensively used; and was lowest in the large villages, P and Sp, in which this foodstuff was used the least. This is undoubtedly due, in our opinion, to a tendency of some families living in pellagrous districts to restrict their use of shipped corn and substitute for it, in whole or in part, local corn-meal. The theories concerning causation of the disease which may be held by the local physicians or by the people themselves also seems to be reflected to some extent in the food data. In respect to frequency of use of local corn-meal in relation to the existence of pellagra, the data indicate no particular connection. The highest percentage of pellagrin families occurred in those using this food rarely or never, but the percentage in those who never used it, namely, 15.4, was practically the same as the general percentage for all families, namely, 15.5. In general those families using local corn-meal daily had pellagra less frequently, but the number of families in this group (namely, 36) is, after all, too small to be of much significance. It does show, however, that families using local corn-meal daily and avoiding shipped meal altogether, nevertheless did suffer from pellagra.

These 866 families were made up of 5,089 persons of whom 194 were pellagrins. The distribution of the 5,089 persons and of the 194 pellagrins in respect to the frequency of use of local corn-meal is shown in Tables 21, 22, 23 and 24.

It is evident that the frequency of use of local corn-meal has no definite consistent relation to the pellagra morbidity. In the whole population of the six villages, the 201 persons using it daily show a somewhat smaller proportionate number of cases than the larger group using it rarely or never. Yet, in two villages, I and P, the highest morbidity was among those using this food daily; in two others, Sa and Sp, the highest morbidity was among those using it habitually, and in the remaining two villages, W and A, those persons using local corn rarely or never had the most pellagra. This food

TABLE 18.—Families Containing One or More Cases of Pellagra, Distributed According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	1	0	1	2	0	0	10	14
W	1	0	0	1	0	0	18	20
P	1	1	0	2	0	0	24	28
Sa	1	4	0	3	1	2	13	24
A	0	0	2	0	0	0	15	17
Sp	0	0	0	4	0	1	26	31
Total..	4	5	3	12	1	3	106	134

TABLE 19.—Summarized Distribution of Families According to Frequency of Use of Local Corn-Meal

Village	Total Families			Pellagrin Families		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	5	23	75	1	2	11
W	8	22	78	1	1	18
P	8	18	197	1	3	24
Sa	10	23	65	1	8	15
A	0	9	73	0	0	17
Sp	5	23	224	0	4	27
Total	36	118	712	4	18	112

TABLE 20.—Pellagrin Families in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	20.0	8.7	14.7	13.6
W	12.5	4.5	23.1	18.5
P	12.5	16.7	12.2	12.6
Sa	10.0	34.8	23.1	24.5
A	....	0.0	23.3	20.7
Sp	0.0	17.4	12.1	12.3
Total.....	11.1	15.3	15.7	15.5

TABLE 21.—Distribution of Total Individuals According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	25	26	8	71	40	13	413	596
W	56	22	4	90	14	0	389	575
P	30	20	21	74	16	5	1,210	1,376
Sa	59	47	8	63	35	20	404	636
A	0	11	18	45	3	7	352	436
Sp	31	20	12	84	37	4	1,282	1,470
Total..	201	146	71	427	145	49	4,050	5,089

TABLE 22.—Distribution of Pellagrins According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	1	0	3	3	0	0	13	20
W	1	0	0	2	0	0	20	23
P	3	1	0	4	0	0	29	37
Sa	1	8	0	3	2	3	23	40
A	0	0	2	0	0	0	25	27
Sp	0	0	0	5	0	1	41	47
Total..	6	9	5	17	2	4	151	194

TABLE 23.—Summarized Distribution According to Frequency of Use of Local Corn-Meal

Village	Total Population			Individual Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	25	137	434	1	3	16
W	56	126	393	1	2	20
P	30	110	1,236	3	5	29
Sa	59	145	432	1	13	26
A	0	59	377	0	0	27
Sp	31	141	1,298	0	5	42
Total	201	718	4,170	6	28	160

was most commonly used in the village Sa, in which pellagra was very prevalent, and was used hardly at all in village A, in which pellagra morbidity was almost as high.

It remains now to study the population free from pellagra at the beginning of the year 1912 and the cases which developed in this population during 1912 and 1913, concerning which we have data in regard to the frequency of use of local corn-meal. The distribution of the total families (875) in this population and of the families in which new cases of pellagra occurred (84) are shown in Tables 25, 26, 27 and 28.

TABLE 24.—Pellagra Morbidity in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	4.00	2.19	3.69	3.36
W	1.79	1.59	5.09	4.00
P	10.00	4.55	2.35	2.69
Sa	1.69	8.97	6.02	6.29
A	....	0.00	7.16	6.19
Sp	0.00	3.55	3.24	3.20
Total.....	2.99	3.96	3.84	3.81

TABLE 25.—Distribution of Total Families According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	5	7	1	11	6	2	75	107
W	8	3	1	16	2	1	79	110
P	8	4	4	12	2	1	192	223
Sa	10	7	2	10	6	3	62	100
A	0	1	2	7	1	3	67	81
Sp	5	4	2	13	7	1	222	254
Total..	36	26	12	69	24	11	697	875

Approximately 80 per cent. of the families here considered did not use local corn-meal, so that the groups using it are composed of only a few families each. It is perfectly evident, however, that new cases of pellagra occurred in one or more families in every group without any definite consistent relation to the frequency of use of local corn-meal.

TABLE 26.—Distribution of Families in which New Cases of Pellagra Occurred in 1912 and 1913, According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	1	0	1	2	1	0	11	16
W	1	0	0	1	0	1	8	11
P	1	0	0	1	0	0	17	19
Sa	0	1	0	0	1	2	8	12
A	0	0	0	0	0	1	9	10
Sp	0	1	0	2	0	0	13	16
Total..	3	2	1	6	2	4	66	84

TABLE 27.—Summarized Distribution of Families According to Frequency of Use of Local Corn-Meal

Village	Total Families			Families with Incident Pellagra		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	5	24	78	1	3	12
W	8	21	81	1	1	9
P	8	18	197	1	1	17
Sa	10	23	67	0	2	10
A	0	9	72	0	0	10
Sp	5	24	225	0	3	13
Total	36	119	720	3	10	71

TABLE 28.—Families with Incident Pellagra in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	20.0	12.5	15.4	15.0
W	12.5	4.8	11.1	10.0
P	12.5	5.6	8.6	8.5
Sa	0.0	8.7	14.9	12.0
A	....	0.0	13.9	12.3
Sp	0.0	12.5	5.8	6.3
Total.....	8.3	8.4	9.9	9.6

In the 875 families just considered, there were 4,999 persons who were not pellagrins, so far as we could ascertain, at the beginning of the year 1912. Of these 4,999 persons, 109 contracted the disease during 1912 and 1913. The distribution according to the use of local corn-meal in their families, of the 4,999 total individuals and of the 109 who became pellagrins in 1912 and 1913, is shown in Tables 29, 30, 31 and 32.

TABLE 29.—Distribution of Individuals According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	25	26	8	71	44	13	440	627
W	56	22	4	89	14	6	381	572
P	28	19	21	72	16	5	1,200	1,361
Sa	58	41	8	60	34	20	401	622
A	0	0	0	0	0	12	352	364
Sp	31	26	12	81	37	3	1,263	1,453
Total..	198	134	53	373	145	59	4,037	4,999

TABLE 30.—Distribution of Incident Pellagrins According to Frequency of Use of Local Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	1	0	3	3	1	0	14	22
W	1	0	0	1	0	3	8	13
P	1	0	0	2	0	0	19	22
Sa	0	2	0	0	1	3	8	14
A	0	0	0	0	0	1	14	15
Sp	0	1	0	2	0	0	20	23
Total..	3	3	3	8	2	7	83	109

There is a suggestion of an inverse relation between the use of local corn-meal and the occurrence of new cases of pellagra in this population as a whole, those using it daily showing an incidence of new cases of 1.52 per cent., whereas those using it rarely or never show an incidence of 2.24 per cent. In village A, in which local corn-meal scarcely entered into the diet, the highest incidence of new cases was

TABLE 31.—Summarized Distribution According to Frequency of Use of Local Corn-Meal

Village	Total Individuals			Incident Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	25	141	461	1	4	17
W	56	125	391	1	1	11
P	28	107	1,226	1	2	19
Sa	58	135	429	0	3	11
A	0	0	364	0	0	15
Sp	31	144	1,278	0	3	20
Total	198	652	4,149	3	13	93

TABLE 32.—Incidence of Pellagra in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	4.00	2.84	3.69	3.51
W	1.79	0.80	2.81	2.27
P	3.57	1.87	1.55	1.62
Sa	0.00	2.22	2.56	2.25
A	....	....	4.12	4.12
Sp	0.00	2.08	1.56	1.58
Total.....	1.52	1.99	2.24	2.18

observed. In two villages, however, namely, I and P, the incidence was highest in the group using local corn-meal daily. Probably several conflicting factors disturb the relationships. In general we believe that people who use local corn daily are likely to be particular about their diet in other respects, and often are in better financial condition than the average of the population. These associated factors would doubtless operate to diminish the incidence of pellagra in this group. On the other hand, certain families, after one of their members has contracted pellagra, not only tend to restrict their use of shipped corn, but in some cases they tend to substitute local corn for it. As we shall see in a subsequent section of this report, the members of such families seem to be especially likely to develop the disease, and this may be a factor in the high incidence in those using this food daily in certain villages. In any event, it is clear that this study of the use of local corn has failed to reveal any consistent relation between it and pellagra.

ANY CORN-MEAL

Corn-meal was used by the vast majority of the population studied. Most of those who never used shipped corn-meal did use local corn-meal. It therefore seems desirable to examine the data concerning the use of any corn-meal. The records in respect to this foodstuff include 858 families present in the six villages at the time of our census in 1913, of which 137 contained one or more cases of pellagra. The distribution of the 858 total families and of the 137 pellagrin families in respect to the use of corn-meal is shown in Tables 33, 34, 35 and 36.

TABLE 33.—DISTRIBUTION OF TOTAL FAMILIES ACCORDING TO FREQUENCY OF USE OF ANY CORN-MEAL

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	63	26	13	0	0	1	2	105
W	67	24	3	0	0	0	0	94
P	137	59	27	0	0	0	2	225
Sa	59	26	14	0	0	0	1	100
A	40	23	19	1	0	0	0	83
Sp	149	49	29	2	1	0	21	251
Total..	515	207	105	3	1	1	26	858

TABLE 34.—FAMILIES CONTAINING ONE OR MORE CASES OF PELLAGRA, DISTRIBUTED ACCORDING TO FREQUENCY OF USE OF ANY CORN-MEAL

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	8	3	3	0	0	0	0	14
W	11	6	2	0	0	0	0	19
P	14	10	5	0	0	0	0	29
Sa	15	7	4	0	0	0	1	27
A	7	5	5	0	0	0	0	17
Sp	16	6	3	2	1	0	3	31
Total..	71	37	22	2	1	0	4	137

Corn-meal was used by all but 26 of the 858 families, and by 515 of these families it was used daily. In one village, Sp, there were 21 families who avoided the use of corn-meal, probably as a prophy-

lactic measure against pellagra. In every one of the six villages the existence of pellagra was relatively less frequent in the families using corn-meal daily than in those using it rarely. This is probably due to a tendency on the part of some pellagrin families to restrict their use of corn-meal. It certainly does not indicate any consistent positive correlation between use of corn-meal and presence of pellagra in these families.

TABLE 35.—Summarized Distribution of Families According to the Use of Any Corn-Meal

Village	Total Families			Pellagrin Families		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	63	26	16	8	3	3
W	67	24	3	11	6	2
P	137	59	29	14	10	5
Sa	59	26	15	15	7	5
A	40	24	19	7	5	5
Sp	149	52	50	16	9	6
Total	515	211	132	71	40	26

TABLE 36.—Pellagrin Families in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	12.7	11.5	18.8	13.3
W	16.4	25.0	66.7	20.2
P	10.2	16.9	17.2	12.9
Sa	25.4	26.9	33.3	27.0
A	17.5	20.8	26.3	20.5
Sp	10.7	17.3	12.0	12.4
Total.....	13.8	19.0	19.7	16.0

These 858 families included 5,095 individuals, of whom 196 were pellagrins. Their distribution in respect to the use of corn-meal is shown in Tables 37, 38, 39 and 40.

It is evident that nearly everybody in these villages used corn-meal to some extent. Only 123 persons were members of families in which this foodstuff was not used and 97 of these persons were in one village, Sp. The inverse relation between the existence of pellagra and the use of corn is clearly shown in Table 40. In every village there were relatively more cases of pellagra in the population using this food rarely or never than in the group using it daily. Of

TABLE 37.—Distribution of Total Individuals According to Frequency of Use of Any Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	381	141	70	0	0	2	6	600
W	415	128	17	0	0	0	0	560
P	850	377	147	0	0	0	11	1,385
Sa	367	183	77	0	0	0	9	636
A	212	152	86	4	0	0	0	454
Sp	910	278	159	9	7	0	97	1,460
Total..	3,135	1,259	556	13	7	2	123	5,095

TABLE 38.—Distribution of Pellagrins According to Frequency of Use of Any Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	12	3	5	0	0	0	0	25
W	14	8	3	0	0	0	0	38
P	18	12	8	0	0	0	1	38
Sa	20	12	5	0	0	0	0	27
A	12	7	8	0	0	0	5	46
Sp	22	9	6	3	1	0	0	20
Total..	98	51	35	3	1	0	6	194

TABLE 39.—Summarized Distribution According to Frequency of Use of Any Corn-Meal

Village	Total Population			Individual Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	381	141	78	12	3	5
W	415	128	17	14	8	3
P	850	377	158	18	12	8
Sa	367	183	86	20	12	6
A	212	156	86	12	7	8
Sp	910	294	256	22	13	11
Total	3,135	1,279	681	98	55	41

the 123 persons recorded as never using corn-meal, six (or 4.9 per cent.) were pellagrins, a relative morbidity greater than that observed in persons using corn-meal daily. It should be noted, however, that this group is made up of persons who were not using corn-meal at the time of the census and had not used it for the preceding two years. Doubtless most if not all these persons had at some time used corn-meal. The information in regard to diet in these tables refers therefore to the diet at the time of observation, namely, 1912 and 1913, and not necessarily to the diet at the time when pellagra originated.

TABLE 40.—Pellagra Morbidity in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	3.15	2.13	6.41	3.33
W	3.37	6.25	17.65	3.46
P	2.12	3.18	5.06	2.74
Sa	5.45	6.56	6.98	5.97
A	5.66	4.49	9.30	5.95
Sp	2.42	4.42	4.30	3.15
Total.....	3.13	4.30	6.02	3.81

TABLE 41.—Distribution of Total Families According to Frequency of Use of Any Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	65	27	13	0	0	1	2	108
W	68	24	4	0	0	0	1	97
P	137	59	27	0	0	0	2	225
Sa	61	26	14	0	0	0	1	102
A	40	23	19	1	0	0	0	83
Sp	150	50	29	2	1	0	21	253
Total..	521	209	106	3	1	1	27	868

The use of any corn-meal by incident cases of pellagra would appear to be of particular interest. The total population of these six mill villages, for which we have available data for a study of this topic, includes 868 families, in 85 of which new cases of pellagra developed in 1912 and 1913. The distribution of these families in respect to the use of any corn-meal is shown in Tables 41, 42, 43 and 44.

TABLE 42.—Distribution of Families in which New Cases of Pellagra Occurred in 1912 or 1913, According to Frequency of Use of Any Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	10	4	2	0	0	0	0	16
W	7	1	1	0	0	0	1	10
P	11	4	5	0	0	0	0	20
Sa	6	4	2	0	0	0	0	12
A	3	4	3	0	0	0	0	10
Sp	10	4	1	0	0	0	2	17
Total..	47	21	14	0	0	0	3	85

TABLE 43.—Summarized Distribution of Families According to Frequency of Use of Any Corn-Meal

Village	Total Families			Families with Incident Pellagra		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	65	27	16	10	4	2
W	68	24	5	7	1	2
P	137	59	29	11	4	5
Sa	61	26	15	6	4	2
A	40	24	19	3	4	3
Sp	150	53	50	10	4	3
Total	521	213	134	47	21	17

TABLE 44.—Families with Incident Pellagra in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	15.4	14.8	12.5	14.8
W	10.3	4.2	40.0	10.3
P	8.0	6.8	17.2	8.9
Sa	9.8	15.4	13.3	11.8
A	7.5	16.7	15.8	12.0
Sp	6.7	7.5	6.0	6.7
Total.....	9.0	9.9	12.7	9.8

The incidence of new cases of pellagra in families shows no consistent relation to the frequency of use of corn-meal by these families. In four villages, W, P, Sa and A, and in the total families in the six villages, the families using corn-meal rarely or never developed new cases of pellagra relatively more frequently than those using this foodstuff daily, whereas in two villages, I and Sp, this relation was reversed. In the 27 families not using corn-meal during 1912 and 1913, there were three (or 11.1 per cent.) in which new cases of pellagra developed. This percentage is very similar to the analogous figures in the groups using corn-meal daily, habitually or rarely, and suggests that frequency of use of corn-meal in 1912 and 1913 had no direct relation to the development of new cases of pellagra in these families.

The 868 families just considered included 5,051 persons who were not pellagrins at the beginning of the year 1912. Of these 5,051 persons, 108 developed the disease during 1912 and 1913. The distribution of these persons according to the frequency of use of any corn-meal is shown in Tables 45, 46, 47 and 48.

TABLE 45.—Distribution of Individuals According to Frequency of Use of Any Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	396	153	69	0	0	2	6	626
W	410	121	20	0	0	0	3	554
P	845	369	145	0	0	0	11	1,370
Sa	365	176	76	0	0	0	8	625
A	206	149	83	0	0	0	0	438
Sp	902	278	156	6	6	0	95	1,443
Total..	3,124	1,246	549	6	6	2	123	5,056

The incidence of new cases of pellagra was highest, in each of the six villages, among those persons using corn-meal rarely or never; and in the total population considered together, the incidence in this group was more than twice that of the group using corn-meal daily. The difference is more pronounced than that shown in the study of the families as units, and this means that families using little or no corn-meal not only developed new cases of pellagra more than the families using this food daily, but also developed multiple cases in the same family more frequently. The figures indicate very clearly that restriction or omission of corn-meal as an article of diet failed as

TABLE 46.—Distribution of Incident Pellagrins According to Frequency of Use of Any Corn-Meal

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	14	4	4	0	0	0	0	22
W	6	1	3	0	0	0	1	11
P	13	4	6	0	0	0	0	23
Sa	6	5	4	0	0	0	0	15
A	6	4	5	0	0	0	0	15
Sp	12	4	3	0	0	0	3	22
Total..	57	22	25	0	0	0	4	108

TABLE 47.—Summarized Distribution According to Frequency of Use of Any Corn-Meal

Village	Total Individuals			Incident Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	396	153	77	14	4	4
W	410	121	23	6	1	4
P	845	369	156	13	4	6
Sa	365	176	84	6	5	4
A	206	149	83	6	4	5
Sp	902	290	251	12	4	6
Total	3,124	1,258	674	57	22	29

TABLE 48.—Incidence of Pellagra in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	3.54	2.61	5.19	3.51
W	1.46	0.83	17.39	1.99
P	1.54	1.08	3.85	1.68
Sa	1.64	2.84	4.76	2.40
A	2.91	2.68	6.02	3.42
Sp	1.33	1.38	2.39	1.52
Total.....	1.82	1.75	4.30	2.14

a prophylactic measure against pellagra in this population and suggest very strongly that it cannot be relied on for the control of pellagra.

The group of the population recorded as never using any corn-meal is of particular interest, and especially those families and the four persons in this group in whom pellagra developed in 1912 and 1913. One of these cases occurred in village W and the other three in village Sp, two of them in one family. The family in village W consisted of a man and wife, both about 65 years old, and three grown daughters. Corn-bread had been a staple article of diet until the summer of 1911, after which time it was no longer used. The youngest daughter, Case 78, developed pellagra in 1910 when she was 17 years old. The oldest daughter, Case 77, developed pellagra in the summer of 1911 when she was 27 years old. Both of these were pellagrins before the period of our observations. In June, 1912, about a year after the exclusion of corn-meal from the diet, the third sister, then aged 25, developed a typical erythema, and a diagnosis of pellagra was made. This recurred in July, 1913, without other symptoms. This case, 668, is regarded as incident in 1912, one year after the exclusion of corn-meal from the diet, and is therefore classed in the group of the population not using corn-meal. In the village Sp there are two families to be considered. One of these consisted of a mother, aged 41, and her son, aged 19. Corn-meal was not used, and our record clearly places this family in the class designated as never using this food. The record does not go into the matter in detail, and we do not know with certainty how long it had been excluded from the diet. The woman, Case 742, developed erythema for the first time in August, 1913, and this was accompanied by digestive disturbance and nervous symptoms. The remaining family consisted of a man and wife and three children. The wife, Case 25, developed pellagra in April, 1910, while residing at Columbia, S. C. She was then 38 years old. At that time she consulted one of the most eminent authorities on pellagra in this country and, at his advice, corn-meal was rigidly excluded from the diet of the whole family and none of it has been allowed in the house since 1910. The family moved to Spartanburg in the fall of 1911. The attack of pellagra recurred in the woman in 1911, 1912 and 1913. Early in June, 1912, two of the children, a girl aged 13 and a boy aged 6, developed typical erythema of the hands, and stomatitis. The boy also showed the eruption on his feet and had some diarrhea. In 1913 the boy remained free from symptoms of the disease, but it recurred in his sister with typical erythema, diarrhea and nervous excitability. These two children have been placed in the class not using corn-meal at the time of incidence of pellagra.

The theory that pellagra is caused by the excessive use of corn-meal is not supported by this study. Although every person in the population here considered probably ate corn-meal at some time in his life, there were found two cases of pellagra in which the use of

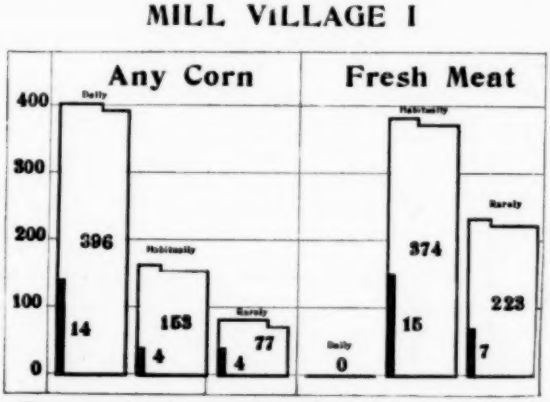


Fig. 9.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

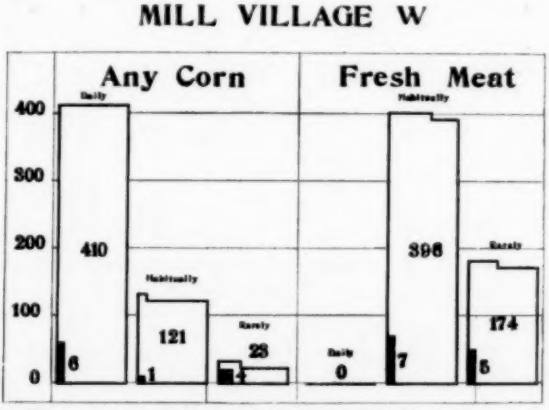


Fig. 10.—The area of each large white column indicattes the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

this foodstuff could be excluded with almost absolute certainty for a period of two years preceding the development of the first sign of the disease, and there were two other cases in which corn-meal had

been excluded from the diet for a year previous to the development of the disease. The total persons in the population studied who have been classed as not using corn-meal amounted to only 123, and it may truly be said that non-pellagrins were placed in this group with much less careful scrutiny than were incident pellagrins. Of these 123 persons, four developed the disease in 1912 and 1913, an incidence of 3.25 per cent. This rate of incidence is greater than that observed among

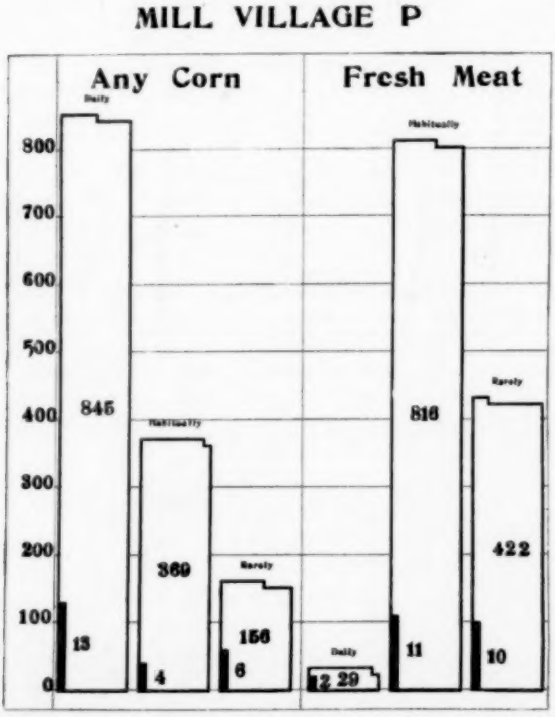


Fig. 11.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

those using corn-meal daily (1.82 per cent.) or habitually (1.75 per cent.). In this population, therefore, the occurrence of new cases of pellagra seems to bear an inverse relation to the frequency of use of corn-meal.

Without committing ourselves to a final opinion, we may offer some suggestions in explanation of these facts. In the first place it seems certain that corn-meal cannot rightly be regarded as the essen-

tial cause of pellagra. The high incidence in those using little corn-meal we believe to be due to their close association with previous pellagra patients. It is chiefly in those families already having one case of pellagra that the use of this food has been intentionally restricted.

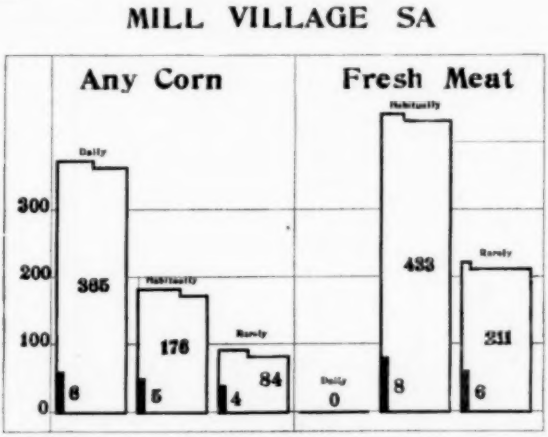


Fig. 12.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

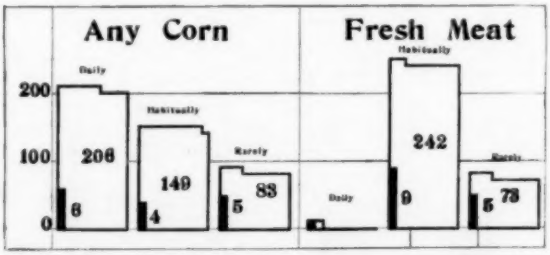


Fig. 13.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

This study has failed to reveal evidence of causal relationship of corn-meal to pellagra, and has shown that restriction of the use of corn-meal in the population studied has not proved effective as a prophylactic measure against pellagra.

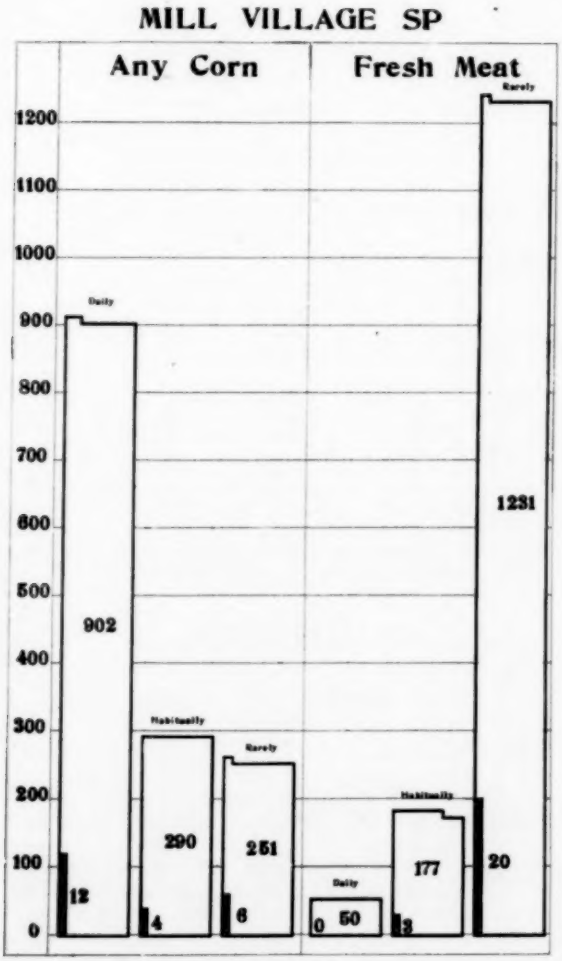


Fig. 14.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

FRESH MEATS

The recorded data in regard to the frequency of use of fresh meat by families present at the time of our census in these six mill villages relate to 861 families, of which 140 then contained one or more cases of pellagra. The distribution of these families according to frequency of use of this food is shown in Tables 49, 50, 51 and 52.

TABLE 49.—Distribution of Total Families According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	14	33	2	40	4	2	95
W	0	6	7	2	52	15	12	94
P	4	88	47	1	65	13	12	230
Sa	0	8	31	0	62	6	0	107
A	1	14	15	2	33	7	11	83
Sp	8	21	204	1	9	0	9	252
Total..	13	151	337	8	261	45	46	861

TABLE 50.—Families Containing One or More Cases of Pellagra, Distributed According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	1	4	0	8	1	0	14
W	0	1	3	0	10	2	3	19
P	1	12	6	0	7	3	1	30
Sa	0	4	9	0	15	1	0	29
A	1	4	4	0	8	0	0	17
Sp	1	1	26	1	2	0	0	31
Total..	3	23	52	1	50	7	4	140

The daily use of fresh meat was rather uncommon in this population, only thirteen families falling in this group. Almost half the families (420) used this food habitually, part time daily or part time habitually, and about half of them (428) used it rarely or never. In two of the villages we failed to find any families in which fresh meat was used daily. The families containing cases of pellagra occur in all the groups and are relatively most numerous in the group using

fresh meat daily and least numerous in the summarized group using this food rarely or never. In those families avoiding fresh meat altogether, only 4 out of a total of 46 had cases of pellagra, or 8.7 per cent., a lower percentage than in any other group.

TABLE 51.—Summarized Distribution of Families According to Frequency of Use of Fresh Meat

Village	Total Families			Pellagrin Families		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	0	56	39	0	9	5
W	0	60	34	0	11	8
P	4	154	72	1	19	10
Sa	0	70	37	0	19	10
A	1	49	33	1	12	4
Sp	8	31	213	1	4	26
Total	13	420	428	3	74	63

TABLE 52.—Pellagrin Families in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	....	16.1	12.8	14.7
W	....	18.3	23.5	20.2
P	25.0	12.3	13.9	13.0
Sa	....	27.1	27.0	27.1
A	100.0	24.5	12.1	20.5
Sp	12.5	12.9	12.2	12.3
Total.....	23.1	17.6	14.7	16.3

The 861 families just considered included 5,133 persons, of whom 199 were pellagrins. The distribution of these persons according to the frequency of use of fresh meat in their families is shown in Tables 53, 54, 55 and 56.

It is evident that only a few (82) persons in this population used fresh meat daily, while 263 did not use it at all. About half the population (2,591 persons) used fresh meat as often as twice a week during part of the year at least, while the remaining population used this food less frequently. In certain mill villages, I, W, Sa and A, fresh meat could be had at local markets in the village only during the colder season of the year; during the summer the inhabitants were com-

TABLE 53.—Distribution of Total Individuals According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	102	182	13	233	28	11	569
W	0	43	43	16	339	70	64	575
P	29	550	281	4	403	73	71	1,411
Sa	0	62	183	0	375	32	0	652
A	2	88	75	23	163	32	67	450
Sp	51	115	1,198	2	60	0	50	1,476
Total..	82	960	1,962	58	1,573	235	263	5,133

TABLE 54.—Distribution of Pellagrins According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	2	7	0	12	1	0	22
W	0	2	6	0	11	2	3	24
P	2	15	10	0	8	3	1	39
Sa	0	6	10	0	18	4	0	38
A	1	8	7	0	11	0	0	27
Sp	1	1	44	1	2	0	0	49
Total..	4	34	84	1	62	10	4	199

TABLE 55.—Summarized Distribution According to Frequency of Use of Fresh Meat

Village	Total Population			Individual Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	0	348	221	0	14	8
W	0	398	177	0	13	11
P	29	957	425	2	23	14
Sa	0	437	215	0	24	14
A	2	274	174	1	19	7
Sp	51	177	1,248	1	4	44
Total	82	2,591	2,460	4	97	98

pelled to get their meat at more distant markets. In the large villages, P and Sp, the local markets sold fresh meat throughout the year. It was in these two villages that the lowest morbidity from pellagra was observed, namely, 2.76 and 3.32 per cent.

TABLE 56.—PELLAGRA MORBIDITY IN EACH OF THE SUMMARIZED GROUPS, PER CENT.

Village	Daily	*Habitually*	*Rarely*	Total
I	....	4.02	3.62	3.87
W	....	3.27	6.21	4.17
P	6.90	2.41	3.29	2.76
Sa	....	5.49	6.51	5.83
A	50.00	6.93	4.02	6.00
Sp	1.96	2.26	3.53	3.32
Total.....	4.88	3.74	3.98	3.88

When we turn our attention to the morbidity in each of the dietary groups, the relation of pellagra to the use of fresh meat is much less evident. In one village, Sp, the morbidity increases progressively with the decrease in frequency of use of fresh meat, daily 1.96, habitually 2.26, rarely 3.53 per cent., but in the same village there were 50 persons who did not use this food at all and none of them had pellagra. In the other villages the correlation is even more confused, and in the total population of the six villages the pellagra morbidity is actually highest in the group of 82 persons who used fresh meat daily, namely, 4.88 per cent., while of the 263 persons who never used it, only 4 suffered from the disease (1.52 per cent.). The recorded data do not seem, therefore, to indicate any consistent correlation between the existence of pellagra and deficiency of fresh meat in the dietary of this population.

The population to be considered in relation to incident cases of pellagra included 884 families, in 85 of which new cases of pellagra developed in 1912 and 1913. The distribution of these families according to frequency of use of fresh meat is shown in Tables 57, 58, 59 and 60.

There is not a consistent correlation between the frequency of use of fresh meat and the origin of new cases of pellagra in these families. In two villages, Sa and Sp, the incidence is highest in the summarized group using fresh meat rarely, but in three villages, I, W and A, it is lowest in this group. In the total families the occurrence of new cases of pellagra seems to be correlated directly with the frequency of use of fresh meat. Even in those 56 families never

TABLE 57.—Distribution of Total Families According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	17	34	2	40	4	12	109
W	0	7	7	2	53	16	12	97
P	4	88	47	1	65	13	12	230
Sa	0	9	31	0	63	6	0	109
A	1	15	15	2	33	7	11	84
Sp	8	22	206	1	9	0	9	255
Total..	13	158	340	8	263	46	56	884

TABLE 58.—Distribution of Families in which New Cases of Pellagra Occurred in 1912 or 1913, According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	4	5	0	6	1	0	16
W	0	2	1	0	6	1	1	11
P	1	7	6	0	4	2	0	20
Sa	0	2	4	0	5	0	0	11
A	1	5	2	0	2	0	0	10
Sp	0	1	15	1	0	0	0	17
Total..	2	21	33	1	23	4	1	85

TABLE 59.—Summarized Distribution of Families According to Frequency of Use of Fresh Meat

Village	Total Families			Families with Incident Pellagra		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	0	59	50	0	10	6
W	0	62	35	0	8	3
P	4	154	72	1	11	8
Sa	0	72	37	0	7	4
A	1	50	33	1	7	2
Sp	8	32	215	0	2	15
Total	13	429	442	2	45	38

using fresh meat, there was only one in which an incident case of pellagra appeared, or 1.8 per cent., a very much lower rate of incidence than was observed in any other group.

In the 884 families just considered, there were 4,853 persons, of whom 109 contracted pellagra in 1912 and 1913. The distribution of these persons according to the frequency of use of fresh meat in their families is shown in Tables 61, 62, 63 and 64.

TABLE 60.—Families with Incident Pellagra in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	....	16.9	12.0	14.7
W	....	12.9	8.6	11.3
P	25.0	7.1	11.1	8.7
Sa	....	9.7	10.8	10.1
A	100.0	14.0	6.1	11.9
Sp	0.0	6.3	7.0	6.7
Total.....	15.4	10.5	8.6	9.6

TABLE 61.—Distribution of Individuals According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	131	184	13	230	28	11	597
W	0	45	38	16	335	74	62	570
P	29	464	280	4	348	72	70	1,267
Sa	0	65	179	0	368	32	0	644
A	2	88	73	0	154	0	0	317
Sp	50	117	1,181	2	58	0	50	1,458
Total..	81	910	1,935	35	1,493	206	193	4,853

New cases of pellagra developed in all the groups, and there is no consistent correlation between the incidence of these cases and the frequenty of use of fresh meat. Of the 81 persons in families using this food daily, 3 acquired pellagra during the two years, a higher incidence (3.70 per cent.) than was observed in any other group. In the 193 persons who did not use fresh meat at all, only 1 new case of pellagra was observed, an incidence of 0.52 per cent., much lower than in any other group. In fact, in the village in which this one case

TABLE 62.—Distribution of Incident Pellagrins According to Frequency of Use of Fresh Meat

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	6	6	0	9	1	0	22
W	0	2	1	0	5	3	1	12
P	2	7	8	0	4	2	0	23
Sa	0	3	6	0	5	0	0	14
A	1	7	5	0	2	0	0	15
Sp	0	2	20	1	0	0	0	23
Total..	3	27	46	1	25	6	1	109

TABLE 63.—Summarized Distribution According to Frequency of Use of Fresh Meat

Village	Total Population			Incident Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	0	374	223	0	15	7
W	0	396	174	0	7	5
P	29	816	422	2	11	10
Sa	0	433	211	0	8	6
A	2	242	73	1	9	5
Sp	50	177	1,231	0	3	20
Total	81	2,438	2,334	3	53	53

TABLE 64.—Incidence of Pellagra in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	....	4.01	3.14	3.69
W	....	1.77	2.87	2.11
P	6.90	1.35	2.37	1.82
Sa	....	1.85	2.84	2.17
A	50.00	3.72	6.85	4.73
Sp	0.00	1.69	1.62	1.58
Total.....	3.70	2.17	2.27	2.25

occurred there were 62 persons who did not use fresh meat, so that the incidence for that village alone was only 1.61 per cent. for this group. One finds here no support for the idea that deficiency of fresh meat in the diet is a cause of pellagra. On the contrary, it would appear quite certain that in the population here studied those avoiding fresh meat contracted this disease least.

TABLE 65.—Distribution of Total Families According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	2	17	58	0	0	0	10	87
W	3	27	48	1	0	0	12	91
P	4	58	136	0	0	1	27	226
Sa	1	21	75	1	0	0	8	106
A	3	21	54	0	0	0	3	81
Sp	3	15	178	0	0	0	54	250
Total..	16	159	549	2	0	1	114	841

TABLE 66.—Families Containing One or More Cases of Pellagra Distributed According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	4	9	0	0	0	0	13
W	0	1	12	1	0	0	3	17
P	0	9	16	0	0	1	5	31
Sa	0	6	20	1	0	0	2	29
A	0	3	14	0	0	0	0	17
Sp	0	0	24	0	0	0	7	31
Total..	0	23	95	2	0	1	17	138

CANNED GOODS

The data in regard to the use of canned goods (tinned foods) include 841 families present at the time of census, 138 of which contained one or more cases of pellagra at that time. The distribution of these families according to frequency of use of tinned foods is shown in Tables 65, 66, 67 and 68.

There is evidently no consistent positive correlation between the frequency of use of canned goods and the existence of cases of pellagra in these families. In fact the indication, if anything, would appear to be the reverse. The 16 families using this kind of food daily had no pellagra, while, of the 114 families avoiding canned goods altogether, no less than seventeen (14.9 per cent.), contained one or more cases of the disease.

TABLE 67.—Summarized Distribution of Families According to Frequency of Use of Canned Goods

Village	Total Families			Pellagrin Families		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	2	17	68	0	4	9
W	3	28	60	0	2	15
P	4	58	164	0	9	22
Sa	1	22	83	0	7	22
A	3	21	57	0	3	14
Sp	3	15	232	0	0	31
Total	16	161	664	0	25	113

TABLE 68.—Pellagrin Families in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	0.0	23.5	13.2	14.9
W	0.0	7.1	25.0	18.7
P	0.0	15.5	13.4	13.7
Sa	0.0	31.8	26.5	27.4
A	0.0	14.3	24.6	21.0
Sp	0.0	0.0	13.4	12.4
Total.....	0.0	15.5	17.0	16.4

The 841 families just considered contained 4,966 persons, of whom 192 were pellagrins. The distribution of these persons according to the frequency of use of tinned foods in their families is shown in Tables 69, 70, 71 and 72.

Evidence of correlation between the existence of pellagra in a family and the frequency of use of canned goods is not to be found in these tables. The 89 persons using canned foods daily had no pellagra. In the 643 persons who avoided such foods, 18, or 2.80 per cent., were pellagrins.

TABLE 69.—Distribution of Total Individuals According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Dailv	Habitually	Rarely		
I	9	111	337	0	0	0	60	517
W	12	168	292	3	0	0	71	546
P	24	416	788	0	0	5	148	1,381
Sa	2	141	462	5	0	0	32	642
A	20	114	286	0	0	0	11	431
Sp	22	88	1,018	0	0	0	321	1,449
Total..	89	1,038	3,183	8	0	5	643	4,966

TABLE 70.—Distribution of Pellagrins According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	5	14	0	0	0	0	19
W	0	1	17	1	0	0	3	22
P	0	12	21	0	0	1	6	40
Sa	0	9	25	2	0	0	2	38
A	0	4	22	0	0	0	0	26
Sp	0	0	40	0	0	0	7	47
Total..	0	31	139	3	0	1	18	192

TABLE 71.—Summarized Distribution According to Frequency of Use of Canned Goods

Village	Total Population			Individual Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	9	111	397	0	5	14
W	12	171	363	0	2	20
P	24	416	941	0	12	28
Sa	2	146	494	0	11	27
A	20	114	297	0	4	22
Sp	22	88	1,339	0	0	47
Total	89	1,046	3,831	0	34	158

For the study of the occurrence of new cases of pellagra in relation to the use of canned goods, we have data on 853 families, in 85 of which one or more new cases of the disease developed in 1912 or 1913. The distribution of these families in respect to frequency of use of tinned foods is shown in Tables 73, 74, 75 and 76.

TABLE 72.—Pellagra Morbidity in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	0	4.55	3.53	3.68
W	0	1.17	5.51	4.03
P	0	2.88	2.98	2.90
Sa	0	7.53	5.47	5.92
A	0	3.51	7.41	6.03
Sp	0	0.00	3.51	3.24
Total.....	0	3.25	4.12	3.87

TABLE 73.—Distribution of Total Families According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	2	17	61	0	1	0	10	91
W	3	27	50	1	0	0	13	94
P	4	58	136	0	0	1	27	226
Sa	1	22	76	1	1	0	8	109
A	3	21	54	0	0	0	3	81
Sp	3	15	180	0	0	0	54	252
Total..	16	160	557	2	2	1	115	853

The occurrence of new cases of pellagra in a family does not appear to have been influenced in any consistent way by the frequency with which the family used canned goods. The 16 families using canned goods daily had no new cases of the disease during the two years. Of the 115 families avoiding the use of these foods, 8 (7 per cent.), had new cases of pellagra during 1912 or 1913.

The 853 families just considered included 4,874 persons, of whom 109 persons contracted pellagra in 1912 or 1913. The distribution of these persons according to frequency of use of tinned foods is shown in Tables 77, 78, 79 and 80.

TABLE 74.—Distribution of Families in which New Cases of Pellagra Occurred in 1912 or 1913, According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	2	12	0	1	0	0	15
W	0	0	9	1	0	0	1	11
P	0	8	10	0	0	1	1	20
Sa	0	2	8	1	1	0	0	12
A	0	2	8	0	0	0	0	10
Sp	0	0	11	0	0	0	6	17
Total..	0	14	58	2	2	1	8	85

TABLE 75.—Summarized Distribution of Families According to Frequency of Use of Canned Goods

Village	Total Families			Families with Incident Pellagra		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	2	18	71	0	3	12
W	3	28	63	0	1	10
P	4	58	164	0	8	12
Sa	1	24	84	0	4	8
A	3	21	57	0	2	8
Sp	3	15	234	0	0	17
Total	16	164	673	0	18	67

TABLE 76.—Families with Incident Pellagra in Total Families in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	0	16.7	16.9	16.5
W	0	3.6	15.9	11.7
P	0	13.8	7.3	8.8
Sa	0	16.7	9.5	11.0
A	0	9.5	14.0	12.3
Sp	0	0.0	7.3	6.7
Total.....	0	11.0	10.0	10.0

TABLE 77.—Distribution of Individuals According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Dailv	Habitually	Rarelv		
I	9	108	367	0	3	0	60	547
W	12	168	291	3	0	0	71	545
P	24	352	778	0	0	5	144	1,303
Sa	2	140	452	5	7	0	32	638
A	20	112	277	0	0	0	0	409
Sp	22	88	1,002	0	0	0	320	1,432
Total..	89	968	3,167	8	10	5	627	4,874

TABLE 78.—Distribution of Incident Pellagrins According to Frequency of Use of Canned Goods

Village	Daily	Habitually	Rarely	Part Time			Never	Total
				Daily	Habitually	Rarely		
I	0	2	18	0	1	0	0	21
W	0	0	11	1	0	0	1	13
P	0	9	11	0	0	1	2	23
Sa	0	2	9	2	1	0	0	14
A	0	2	13	0	0	0	0	15
Sp	0	0	17	0	0	0	6	23
Total..	0	15	79	3	2	1	9	109

TABLE 79.—Summarized Distribution According to Frequency of Use of Canned Goods

Village	Total Individuals			Incident Pellagrins		
	Daily	*Habitually*	*Rarely*	Daily	*Habitually*	*Rarely*
I	9	111	427	0	3	18
W	12	171	362	0	1	12
P	24	352	927	0	9	14
Sa	2	152	484	0	5	9
A	20	112	277	0	2	13
Sp	22	88	1,322	0	0	23
Total	89	986	3,799	0	20	89

TABLE 80.—Incidence of Pellagra in Each of the Summarized Groups, Per Cent.

Village	Daily	*Habitually*	*Rarely*	Total
I	0	2.73	4.22	3.84
W	0	5.85	3.31	2.39
P	0	2.56	1.51	1.77
Sa	0	3.29	1.86	2.19
A	0	1.79	4.69	3.67
Sp	0	0.00	1.74	1.61
Total.....	0	2.03	2.34	2.24

There is no evident consistent correlation discovered here between the use of canned goods and the development of new cases of pellagra. The 89 persons in families using these foods daily remained free from pellagra. Of the 627 persons who avoided altogether the use of canned goods, 9, or 1.44 per cent., developed the disease in the course of the two years 1912 and 1913. There is no significant difference in incidence of pellagra between the groups using these foods habitually and the groups using them rarely. This study has failed therefore to discover any evidence that the use of canned goods causes pellagra, and suggests that these foods had no part in the causation of this disease in this particular population.

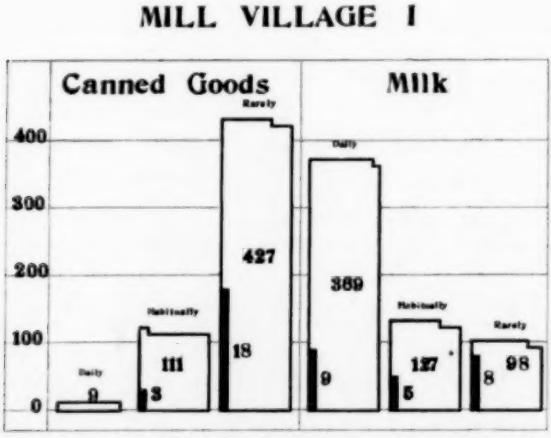


Fig. 15.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

MILL VILLAGE W

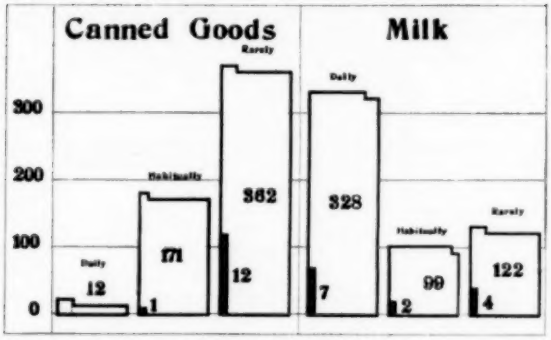


Fig. 16.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

MILL VILLAGE P

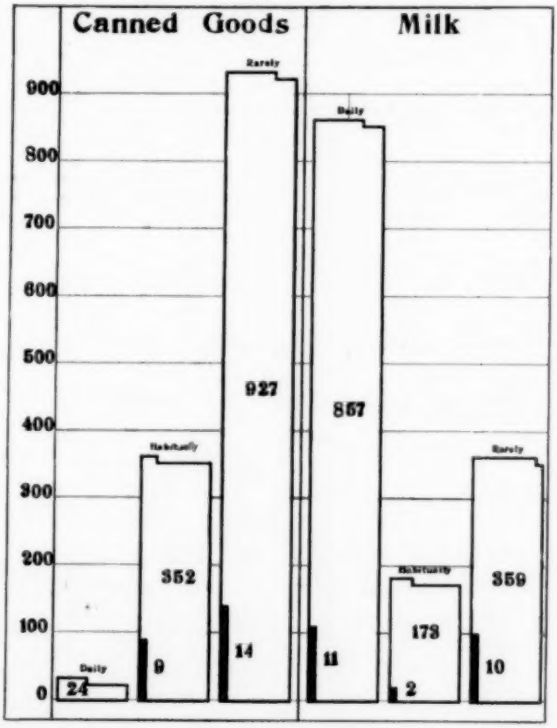


Fig. 17.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

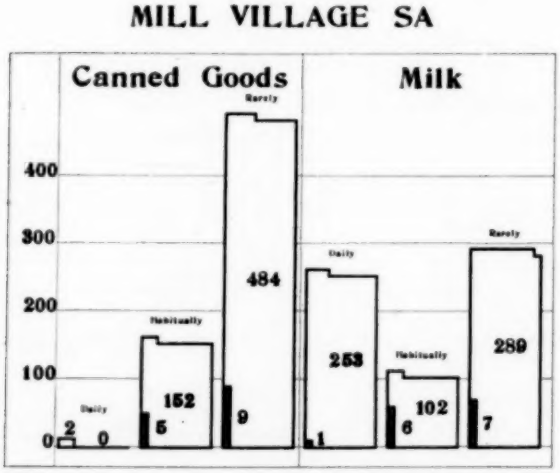


Fig. 18.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

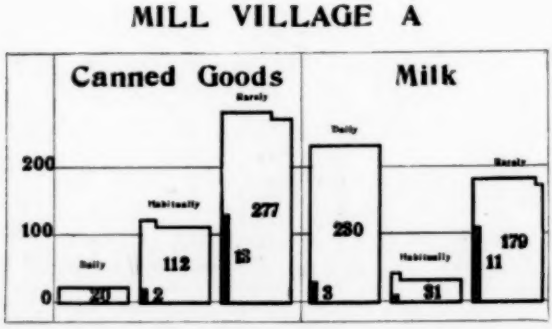


Fig. 19.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

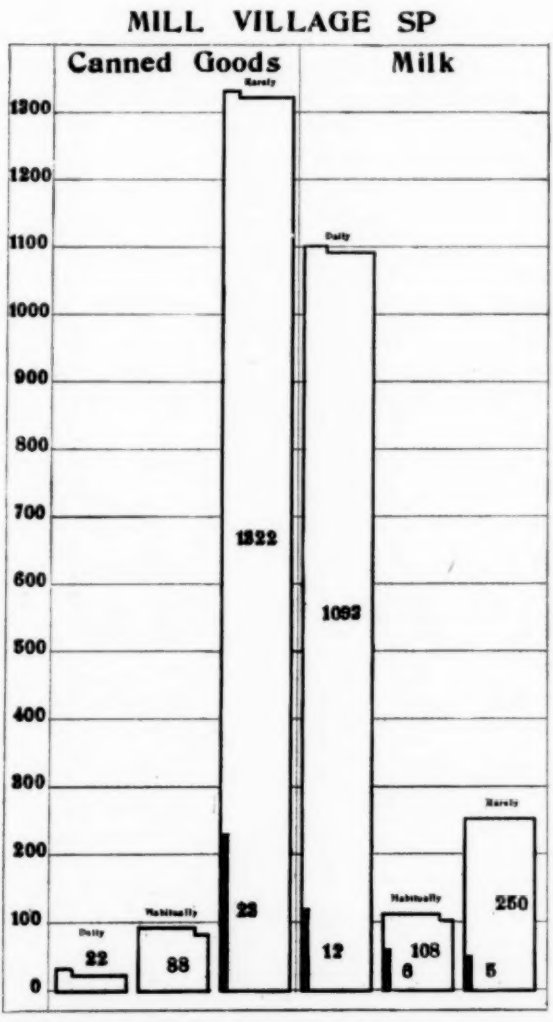


Fig. 20.—The area of each large white column indicates the number of non-pellagrin individuals using the food daily, *habitually* or *rarely*. The included black column indicates the portion of the respective group which contracted pellagra in 1912 or 1913.

MILK

Of the six mill villages used for the detailed study of the foods, only one, Sp, had a market dairy. In the other five villages the families using milk daily kept their own cows, as a rule. In only a few instances was milk purchased daily from neighboring families. Those who used milk less frequently did not possess cows. In many families using milk daily, this food was taken as a beverage in the form of buttermilk. Drinking of sweet milk was very exceptional.

TABLE 81.—DISTRIBUTION OF FAMILIES ACCORDING TO FREQUENCY OF USE OF MILK

Village	Total Families					Pellagrin Families				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	63	21	10	2	96	9	3	0	2	14
W	53	17	8	14	92	7	5	1	6	19
P	137	32	40*	21	230	16	6	5*	4	31
Sa	46	16	18	27	107	13	5	4	7	29
A	39	7†	13	24	83	6	3†	4	4	17
Sp	187	18	29	22	256	20	3	2	6	31
Total	525	111	118	110	864	71	25	16	29	141

* Includes one family using milk part time rarely. † Includes one family using milk part time habitually.

TABLE 82.—PELLAGRIN FAMILIES IN TOTAL FAMILIES IN EACH OF THE GROUPS, PER CENT.

Village	Daily	Habitually	Rarely	Never	Rarely or Never*	Total
I	14.3	14.3	0.0	100.0 42.9	16.7 31.8	14.6 20.7
W	13.2	29.4	12.5	19.0	14.8	13.5
P	11.7	18.8	12.5	25.9	24.4	27.1
Sa	28.3	31.3	22.2	16.7	21.6	20.5
A	15.4	42.9	30.8	27.3	15.7	12.1
Sp	10.7	16.7	6.9			
Total	13.5	22.5	13.6	26.4	19.7	16.3

* This group corresponds to the one designated as *Rarely* in the preceding summary tables.

The recorded data concerning the population present at the time of our census relate to 864 families, in 141 of which one or more cases of pellagra existed at the time. The distribution of these families in respect to the frequency of use of milk is shown in Tables 81 and 82. Only one family used milk part time habitually; one, part time rarely, and none part time daily. These groups are therefore not given separate consideration in the tables.

Milk was used daily by considerably more than half the total families; and in only two of the villages, Sa and A, was this food daily used by less than half the population. The groups using milk habitually, rarely and never are well represented, each including more than 100 families. Table 82 (of percentages) suggests that pellagra was, on the whole, somewhat less common in families using milk daily. Furthermore, the 110 families avoiding altogether the use of milk included 29, or 26.4 per cent., in which pellagra existed, a figure distinctly above the average for the total families considered.

TABLE 83.—Distribution According to Frequency of Use of Milk

Village	Total Populattion					Individual Pellagrins				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	371	127	53	13	564	11	5	0	4	20
W	327	102	55	69	553	9	7	1	7	24
P	865	177	233*	134	1,409	19	6	7†	8	40
Sa	268	103	126	159	656	16	7	7	8	38
A	236	40‡	46	129	451	9	6§	4	8	27
Sp	1,104	104	144	115	1,467	25	7	6	8	46
Total	3,171	653	657	619	5,100	89	38	25	43	195

* Includes five persons using milk part time rarely. † Includes one person using milk part time rarely. ‡ Includes eight persons using milk part time habitually. § Includes one person using milk part time habitually.

TABLE 84.—Pellagra Morbidity in Each of the Groups, Per Cent.

Village	Daily	Habitually	Rarely	Never	Rarely or Never*	Total
I	2.96	3.94	0.00	3.08	6.06	3.55
W	2.75	6.86	1.82	10.14	6.45	4.34
P	2.20	3.39	3.00	5.97	4.09	2.84
Sa	5.97	6.80	5.56	5.03	5.26	5.79
A	3.81	15.00	8.70	6.20	6.86	5.99
Sp	2.26	6.73	4.17	6.96	5.41	3.14
Total	2.81	5.82	3.81	6.95	5.33	3.82

* This group corresponds to the one designated as *Rarely* in the preceding summary tables.

The 864 families just considered included 5,100 persons, of whom 195 were pellagrins at the time of our census. Inasmuch as the four groups using milk daily, habitually, rarely and never each contain more than 600 individuals, while the other groups are very small, it seems best to present the figures in four groups (Tables 83 and 84).

The correlation between frequency of use of milk and freedom from pellagra is not definitely consistent; but, in five of the villages, those avoiding the use of milk altogether had relatively more pellagra than those using this food daily. The figures for the total population also show a marked difference, 2.81 per cent. of those using milk daily being pellagrins against 6.95 per cent. of those never using milk. It would appear, therefore, that pellagrins used milk somewhat less frequently, on the whole, than the population which was free from this disease.

For the study of the relation of milk in the diet to the origin of new cases of pellagra, we have records of 877 families of which 86 developed one or more incident cases of the disease in 1912 or 1913. There were no families in the groups "Part Time Daily" and "Part Time Habitually," and only one family of five persons in the group "Part Time Rarely." It therefore seems unneccessary to present the usual detailed tables of the seven groups. In Tables 85 and 86 the one family of five persons using milk part time rarely has been classed with those using milk rarely. One new case of pellagra developed in this family.

TABLE 85.—Distribution of Families According to Frequency of Use of Milk

Village	Total Families					Families with Incident Pellagra				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	63	21	11	5	100	8	3	1	4	16
W	54	18	9	14	95	5	2	1	3	11
P	137	32	40*	23	232	10	2	2*	6	20
Sa	46	16	19	28	109	1	5	2	4	12
A	39	6	13	25	83	3	1	1	5	10
Sp	188	19	29	22	258	9	4	2	2	17
Total	527	112	121	117	877	36	17	9	24	86

* Includes one family using milk rarely for part of the year only.

In Table 86 the group designated "Rarely or Never" is strictly comparable with the summarized group designated as *Rarely* in the presentation of data concerning other foods. There is a fairly consistent correlation shown in this table, indicating that the families in which milk was not used were the ones in which new cases of pellagra most commonly appeared, while, on the other hand, those families using this food daily developed new cases the most infrequently. This difference would appear to have some significance.

The 877 families just considered included 5,067 persons free from pellagra at the beginning of 1912. Of these 5,067 persons, 110 con-

tracted the disease during 1912 and 1913. One family of five persons used milk rarely for part of the year only. All the other persons fell strictly within the groups shown in Tables 87 and 88.

TABLE 86.—Families with Incident Pellagra in Total Families in Each of the Groups, Per Cent.

Village	Daily	Habitually	Rarely	Never	Rarely or Never	Total
I	12.7	14.3	9.1	80.0	31.3	16.0
W	9.3	11.1	11.1	21.4	17.4	11.6
P	7.3	6.3	5.0	26.1	12.7	8.6
Sa	2.2	31.3	10.5	14.3	12.8	11.0
A	7.7	16.7	7.7	20.0	15.8	12.0
Sp	4.8	21.1	6.9	9.1	7.8	6.6
Total	6.8	15.2	7.4	20.5	13.9	9.8

TABLE 87.—Distribution According to Frequency of Use of Milk

Village	Total Individuals					Incident Pellagrins				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	369	127	56	42	594	9	5	1	7	22
W	328	99	57	65	549	7	2	1	3	13
P	857	173	228*	131	1,389	11	2	2†	8	23
Sa	253	102	127	162	644	1	6	2	5	14
A	230	31	43	136	440	3	1	1	10	15
Sp	1,093	108	141	109	1,451	12	6	3	2	23
Total	3,130	640	652	645	5,067	43	22	10	35	110

* Includes five persons using milk part time rarely. † Includes one person using milk part time rarely.

TABLE 88.—Incidence of Pellagra in Each of the Groups, Per Cent.

Village	Daily	Habitually	Rarely	Never	Rarely or Never	Total
I	2.44	3.94	1.79	16.67	8.16	3.70
W	2.13	2.02	1.75	4.62	3.28	2.37
P	1.28	1.16	0.88	6.11	2.79	1.66
Sa	0.40	5.88	1.57	3.09	2.42	2.17
A	1.30	3.23	2.33	7.35	6.15	3.41
Sp	1.09	5.56	2.13	1.84	2.00	1.59
Total	1.37	3.44	1.53	5.43	3.47	2.17

It is evident that in the whole population those persons using milk daily contracted pellagra the least. Of the 3,130 persons in this group, only 43 acquired the disease during the two years. In the whole population also, it is clear that those avoiding the use of milk suffered most from the development of new cases of pellagra. The incidence of the disease in the latter group, 5.43 per cent., is nearly four times that in the former, 1.37 per cent. In every one of the six villages the group using milk daily showed a lower incidence than the average for that village, and those never using milk showed a higher incidence than the average. The correlation is quite inconsistent in the groups using milk habitually and rarely. The tendency toward correlation between the occurrence of new cases of pellagra and the deficiency of milk in the diet is nevertheless distinctly evident, on the whole, and suggests that the use of milk (including buttermilk) as a food has some value in the prevention of pellagra.

TABLE 89.—Distribution of Families According to Frequency of Use of Eggs

Village	Total Families					Pellagrin Families				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	37	42	13	0	92	3	6	2	0	11
W	14	52	23	6	95	3	7	8	1	19
P	35	125	55	9	224	3	17	5	1	26
Sa	26	46	31	3	106	10	9	9	1	29
A	13	35*	30	5	83	1	8*	8	0	17
Sp	28	90	129	5	252	2	14	14	1	31
Total	153	390	281	28	852	22	61	46	4	133

*Includes one family using eggs part time habitually.

EGGS

The recorded data concerning the use of eggs relate to 852 families present in the six villages at the time of our census, of which 133 contained one or more pellagrins. The distribution of these families according to the frequency of use of eggs is shown in Tables 89 and 90.

The tabulated data show very clearly that there was no significant variation in existence of pellagra in families correlated with a difference in frequency of use of eggs. The percentage of families with pellagra in the different groups is remarkably uniform.

The 852 families contained 5,068 persons, of whom 186 were pellagrins at the time of our census. The distribution of these persons according to frequency of use of eggs in their families, is shown in Tables 91 and 92.

TABLE 90.—Pellagrin Families in Total Families in Each of the Groups, Per Cent.

Village	Daily	Habitually	Rarely	Never	Rarely or Never	Total
I	8.1	14.3	15.4	....	15.4	12.0
W	21.4	13.5	34.8	16.7	31.0	20.0
P	8.6	13.6	9.1	11.1	9.4	11.6
Sa	38.5	19.6	29.0	33.3	29.4	27.4
A	7.7	22.9	26.7	0.0	22.9	20.5
Sp	7.1	15.6	10.9	20.0	11.2	12.3
Total	14.4	15.6	16.4	14.3	16.2	15.6

TABLE 91.—Distribution According to Frequency of Use of Eggs

Village	Total Population					Individual Pellagrins				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	225	253	64	0	542	3	9	4	0	16
W	75	317	144	32	568	5	8	10	1	24
P	198	786	337	62	1,383	3	22	8	1	34
Sa	157	267	209	19	652	15	9	13	1	38
A	65	187*	169	28	449	1	16†	10	0	27
Sp	151	505	789	29	1,474	3	15	27	2	47
Total	871	2,315	1,712	170	5,068	30	79	72	5	186

* Includes eight persons using eggs part time habitually. † Includes four persons using eggs part time habitually.

TABLE 92.—Pellagra Morbidity in Each of the Groups, Per Cent.

Village	Daily	Habitually	Rarely	Never	Rarely or Never	Total
I	1.33	3.56	6.25	....	6.25	2.95
W	6.67	2.52	6.94	3.13	6.25	4.23
P	1.52	2.80	2.37	1.61	2.26	2.46
Sa	9.55	3.37	6.22	5.26	6.14	5.83
A	1.54	8.56	5.99	0.00	5.13	6.01
Sp	1.99	2.97	3.42	6.90	3.55	3.19
Total	3.44	3.41	4.21	2.94	4.09	3.67

It is evident from the tables that no consistent correlation has been discovered between the distribution of cases of pellagra and the frequency of use of eggs.

In regard to the relation between use of eggs and the origin of new cases of pellagra, we have data on 861 families, of which 77 developed one or more new cases in 1912 or 1913. The distribution according to frequency of use of eggs is shown in Tables 93 and 94.

TABLE 93.—Distribution of Families According to Frequency of Use of Eggs

Village	Total Families					Families with Incident Pellagra				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	38	43	13	0	94	3	7	2	0	12
W	15	53	24	6	98	2	5	4	0	11
P	37	125	55	9	226	5	9	3	0	17
Sa	27	47	31	3	108	4	2	5	1	12
A	13	34	30	6	83	0	5	4	1	10
Sp	28	90	129	5	252	1	8	5	1	15
Total	158	392	282	29	861	15	36	23	3	77

TABLE 94.—Families with Incident Pellagra in Total Families in Each of the Groups, Per Cent.

Village	Daily	Habitually	Rarely	Never	Rarely or Never	Total
I	7.9	16.3	15.4	....	15.4	12.8
W	13.3	9.4	16.7	0.0	13.3	11.2
P	13.5	7.2	5.5	0.0	4.7	7.5
Sa	14.8	4.3	16.1	33.3	17.6	11.1
A	0.0	14.7	13.3	16.7	13.9	12.0
Sp	3.6	8.9	3.9	20.0	4.5	6.0
Total	9.5	9.2	8.2	10.3	8.4	8.9

There is no evidence of any relationship between the use of eggs by a family and the development of a new case of pellagra in that family.

The 861 families just considered included 4,724 persons free from pellagra at the beginning of 1912. Of these 4,724 persons, 99 contracted the disease during 1912 and 1913. The distribution of these persons according to frequency of use of eggs in their families is shown in Tables 95 and 96.

In these tables it again appears that pellagra originated with almost equal frequency in all the groups, and there is no evidence that its origin was influenced at all by the presence or absence of eggs in the diet. The high incidence, 3.43 per cent., in the 175 persons never using eggs does not appear worthy of much consideration because of the small number of persons concerned and the irregularity of the figures for the different villages.

TABLE 95.—Distribution According to Frequency of Use of Eggs

Village	Total Families					Incident Pellagrins				
	Daily	Habitually	Rarely	Never	Total	Daily	Habitually	Rarely	Never	Total
I	235	256	64	0	555	4	9	4	0	17
W	15	80	140	31	266	2	7	4	0	13
P	210	774	333	61	1,378	5	10	4	0	19
Sa	153	266	202	19	640	5	2	6	1	14
A	64	174	163	36	437	0	7	4	4	15
Sp	149	499	772	28	1,448	1	9	10	1	21
Total	826	2,049	1,674	175	4,724	17	44	32	6	99

TABLE 96.—Incident Pellagrins in Total Population in Each Group, Per Cent.

Village	Daily	Habitually	Rarely	Never	Rarely or Never	Total
I	1.70	3.52	6.25	....	6.25	3.06
W	13.33	8.75	2.86	0.00	2.34	4.89
P	2.38	1.29	1.20	0.00	1.02	1.38
Sa	3.27	0.75	2.97	5.26	3.17	2.19
A	0.00	4.02	2.45	11.11	4.02	3.43
Sp	0.67	1.80	1.30	3.57	1.38	1.45
Total	2.06	2.15	1.91	3.43	2.06	2.10

THE RELATION BETWEEN LOCATION OF A DOMICILE OF AN INCIDENT CASE OF PELLAGRA AND THE DOMICILE OF AN ANTECEDENT CASE

The data accumulated by the house-to-house census in the various mill villages, and our records of the cases of pellagra there, permit us to examine the geographical relationship of the houses in which pellagra has developed to houses in which a case of the disease already existed. We have chosen to divide the non-pellagrin population of

MILL VILLAGE I

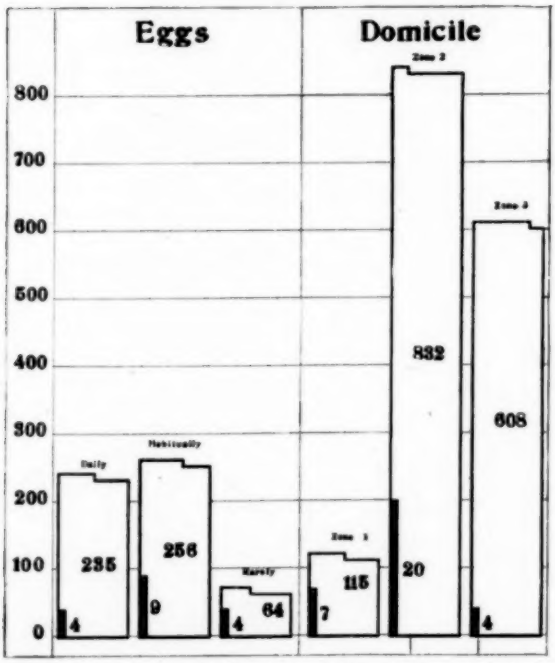


Fig. 21.—The area of each of the three white columns at the left indicates the number of non-pellagrin individuals using eggs daily, *habitually* and *rarely*. The three columns at the right indicate in the same way the number of non-pellagrin individuals living in each of the three domiciliary zones. The included black column indicates in each instance the portion of the respective group which contracted pellagra in 1912 or 1913.

MILL VILLAGE W

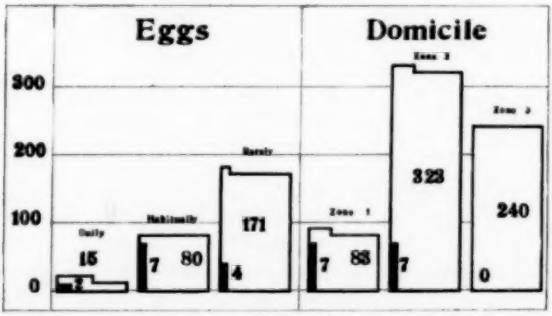


Fig. 22.—The area of each of the three white columns at the left indicates the number of non-pellagrin individuals using eggs daily, *habitually* and *rarely*. The three columns at the right indicate in the same way the number of non-pellagrin individuals living in each of the three domiciliary zones. The included black column indicates in each instance the portion of the respective group which contracted pellagra in 1912 or 1913.

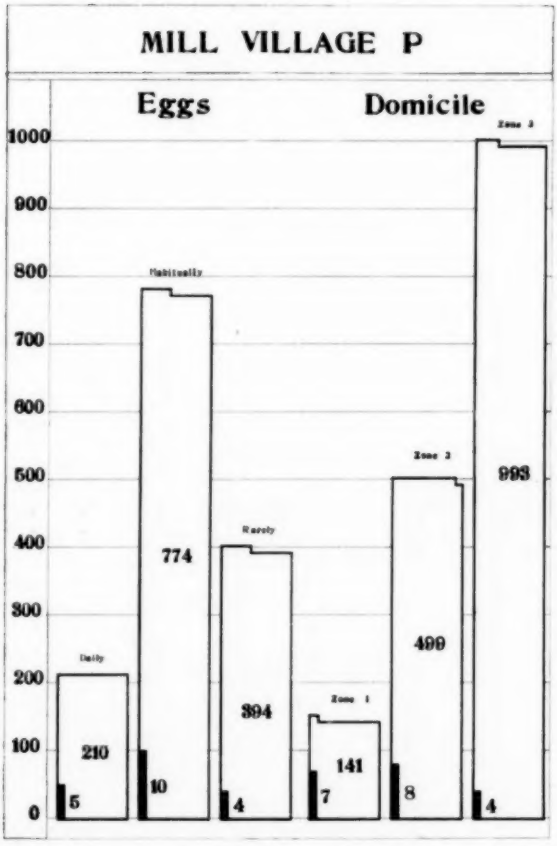


Fig. 23.—The area of each of the three white columns at the left indicates the number of non-pellagrin individuals using eggs daily, *habitually* and *rarely*. The three columns at the right indicate in the same way the number of non-pellagrin individuals living in each of the three domiciliary zones. The included black column indicates in each instance the portion of the respective group which contracted pellagra in 1912 or 1913.

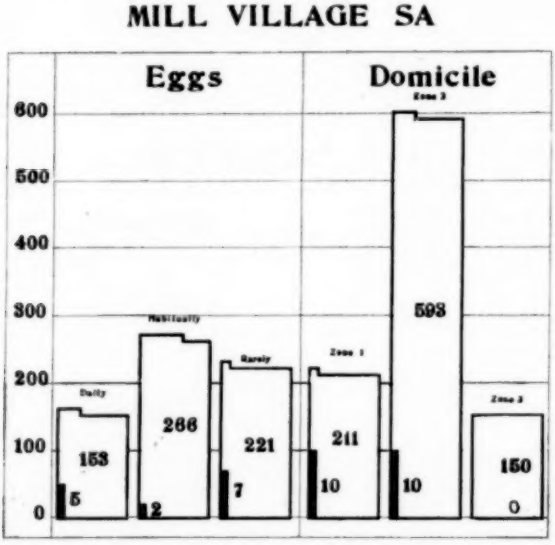


Fig. 24.—The area of each of the three white columns at the left indicates the number of non-pellagrin individuals using eggs daily, *habitually* and *rarely*. The three columns at the right indicate in the same way the number of non-pellagrin individuals living in each of the three domiciliary zones. The included black column indicates in each instance the portion of the respective group which contracted pellagra in 1912 or 1913.

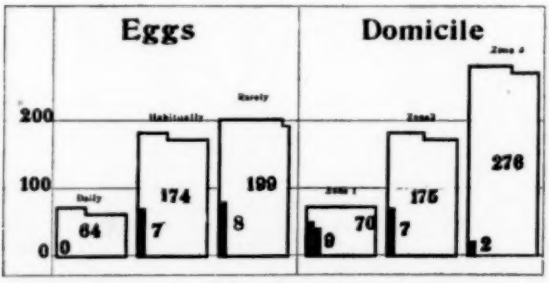


Fig. 25.—The area of each of the three white columns at the left indicates the number of non-pellagrin individuals using eggs daily, *habitually* and *rarely*. The three columns at the right indicate in the same way the number of non-pellagrin individuals living in each of the three domiciliary zones. The included black column indicates in each instance the portion of the respective group which contracted pellagra in 1912 or 1913.

each village into three parts or zones in respect to domicile: first zone, those persons free from pellagra living in the same building in which a patient with pellagra resided during 1912 or the first part of 1913; second zone, those persons, not included in the first zone, who resided in a house adjacent to the house of a pellagrin; third zone, those persons living in houses at distances greater than next door to the domicile of a pellagrin. The second zone included the houses

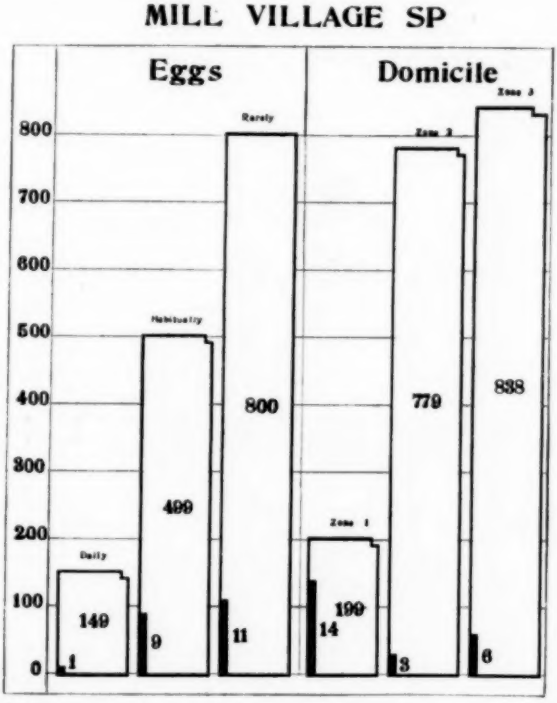


Fig. 26.—The area of each of the three white columns at the left indicates the number of non-pellagrin individuals using eggs daily, *habitually* and *rarely*. The three columns at the right indicate in the same way the number of non-pellagrin individuals living in each of the three domiciliary zones. The included black column indicates in each instance the portion of the respective group which contracted pellagra in 1912 or 1913.

at either side, directly in front, across the street, and directly behind, provided the intervening space was not greater than that of the ordinary mill-village lot (about 100 feet) and also the four houses adjacent on diagonals from the original house. The scheme of the study may be quickly grasped by reference to Figure 27. Each house containing a patient with pellagra during 1912 or early in 1913, whether the

patient moved in there or the case originated there, was considered in turn as the center of such a diagram, and the total persons free from pellagra at the beginning of exposure ascertained for each case as far as our records show them. By adding together the totals for each zone we were then able to ascertain the total number of non-pellagrin population living in the same house with a pellagrin and the total number of cases of pellagra known to develop in this population during 1912 and 1913; in the same way the total number of instances in which

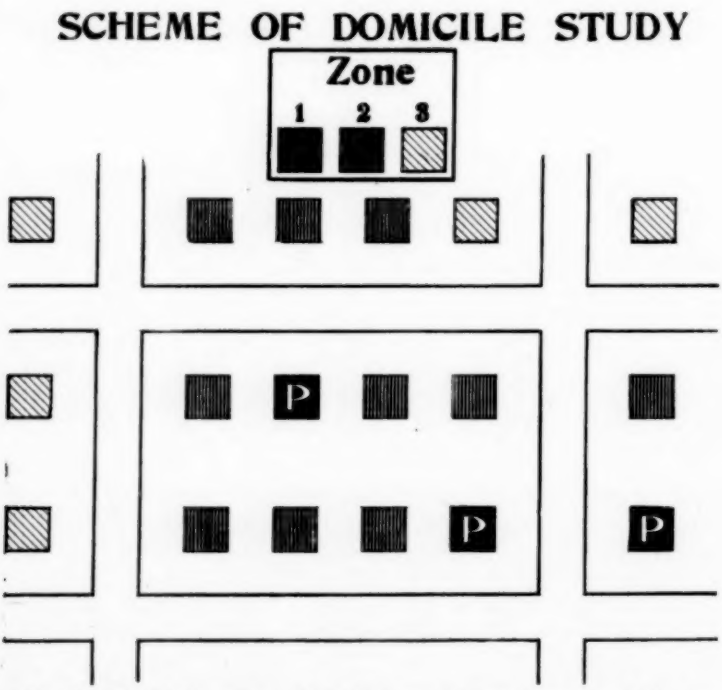


Fig. 27.—The black squares with white letters indicate houses in which cases of pellagra already existed. These houses belong to Zone 1. Houses situated next door belong to Zone 2. All houses situated farther away belong to Zone 3.

a person free from the disease had been domiciled next door to a case of pellagra and total number of instances in which pellagra had arisen under these circumstances; and in the same way for the third zone, we were able to ascertain the number of persons living at a greater distance than next door from a case of pellagra and the total instances in which pellagra had developed during 1912 and 1913 in this population.

Certain difficulties presented themselves from time to time in making this statistical study. It was essential that our knowledge of the cases and of the population employed should be very complete. We therefore limited the antecedent cases to be used to known pellagrins and we excluded from this study those pellagrins who had shown no symptoms of the disease for two years. It was also decided to omit from consideration mere visitors, provided the duration of the visit were less than two weeks. Furthermore, we did not consider as antecedent cases those pellagrins who had moved into the village or had developed symptoms of the disease for the first time within a period of three months preceding the time of our census and search for cases.

Certain arbitrary rules had to be adopted also in regard to the exposed population. Zone 1 included all non-pellagrins known to have lived in the same house with an antecedent case, as defined above, for a period of at least two weeks during 1912 or 1913. Cases of pellagra developing in this zone were considered as incident cases possibly secondary to the antecedent case only when the disease developed after an interval of at least two weeks from the beginning of the domiciliary relationship and within three months in summer or six months in the colder season after the termination of such relationship. Zone 2 included the non-pellagrins living in a house next door to an antecedent case. Those persons who lived next door to several houses in which pellagra existed were considered in relation to each of these houses in turn and added to the population of Zone 2 each time. The population of Zone 2 does not, therefore, mean the number of different persons living next door to a pellagrin, but it designates the number of instances in which a non-pellagrin lived next door to a house containing a pellagrin for a period of at least two weeks during the years selected. Incident cases of pellagra developing in Zone 2 were regarded as possibly secondary to the antecedent case only when symptoms of the disease developed not earlier than two weeks from the beginning of the supposed exposure and not later than from three to six months after its termination. Cases developing in Zone 2 next door to two or more houses containing antecedent cases were credited as secondary to each such case, so that the incident cases in Zone 2 represent not the actual number of persons developing the disease in this zone but the number of instances in which this relationship was followed by the development of incident pellagra. As explained above, the persons who did not contract the disease were treated in a similar way in compiling the statistics. Finally, Zone 3 included all the population living for a period of at least three months in spring and summer or six months in the colder season in houses farther removed than next door from any known case of pellagra;

and any case of pellagra developing in such persons, or in any one not falling within Zone 1 or Zone 2, according to our arbitrary rules, was credited to Zone 3. New cases of pellagra definitely recorded as such, concerning which our information was too incomplete to warrant a final placing in one of these zones, have been temporarily placed in Zone 3. Obviously, it would sometimes happen that a person would first be in Zone 3 and later come to be included in one of the other zones because of change of residence on his part or because a pellagrin would appear next door to him or in his own household. It seemed necessary to adopt such arbitrary rules and to adhere to them throughout this statistical study. Our purpose, of course, was to ascertain whether the proximity of residence to cases of pellagra would show any correlation to the incidence of the disease in these mill villages.

TABLE 97.—Domicile Relationship, Village I, Zone 1

Antecedent Case Present Between October, 1911, and June, 1913			Other Members of the Household			
Case	House	Residence Period	Adults	Children	Total	Incident Pellagrins
514	39	Dec., 1911-May, 1912	17	5	22	1
114	41	Apr., 1911-July, 1913	4	1	5	0
145	44	Jan., 1912-July, 1913	3	3	6	2
148 } 149 }	40	1910-July, 1913	3	3	6	1
337	617	Apr. '12-Mar. 31, '13	2	3	5	0
592	617	Mar. 31, '13-July, '13	2	3	5	0
280	611	Feb., 1913-July, 1913	1	1	2	0
330	66	Jan., 1911-July, 1913 Pellagra developed July, 1912	3	4	7	0
164	59	Mar., 1910-July, 1913	1	4	5	0
153 } 154 }	54	Nov., 1911-July, 1913	2	2	4	1
150	48	July, 1912-Sept., 1912	12	2	14	1
Total for this portion of the table.....			50	31	81	6

The method of procedure in this study may be illustrated by a sample portion of the original tabulations, from which the data concerning exact location of each house have been purposely omitted (Tables 97, 98 and 99). These fragments of our detailed tables indicate the method employed in compiling the data. It is impossible to print here the complete tabulations because of their extent. The summary of these data is shown in Table 100.

TABLE 98.—Domicile Relationship, Village I, Zone 2

Antecedent Case Present Between October, 1911, and June, 1913			Population Resident in Adjacent Houses				
Case	House	Residence Period	Residence Period	Adults	Children	Total	Incident Pellagrins
514	39	Dec., 1911-May, 1912	Dec., 1911-July, 1913	2	1	3	0
			May, 1912-Sept. 10, 1912	2	1	3	0
			May, 1911-July, 1913	3	2	5	0
			Feb., 1909-July, 1913	2	3	5	0
			Total	9	7	16	0
114	41	Apr., 1911 - July, 1913	Apr. 1908-July, 1913	2	1	3	0
			Feb., 1913-July, 1913	3	0	3	0
			Antecedent Pellagra in Household	..	..	..	..
			Nov., '11 - July, 1913	2	4	6	0
			Jan., 1910-July, 1913	3	1	4	0
			Feb., 1909-July, 1913	2	3	5	0
			Oct., 1912-July, 1913	5	3	8	0
			Total	17	12	29	0
145	44	Jan., 1912-July, 1913	Mar., '12 - Feb., 1913	4	4	8	0
			Jan. 1911-July, 1913	3	5	8	2
			Mar., '13-July, 1913	4	0	4	0
			Feb., 1913-July, 1913	3	0	3	0
			Dec., 1912-July, 1913	3	4	7	0
			Aug., '12-Mar., 1913	5	5	10	0
			June, '13,-July, 1913	2	0	2	0
			Antecedent Pellagra in Household	..	..	..	..
			Apr., 1913-July, 1913	2	2	4	0
			Mar., '13-July, 1913	2	0	2	0
			Apr., 1913-July, 1913	2	1	3	0
			Dec., '11-Mar., 1913	3	0	3	0
			July, '12-Mar., 1913	5	4	9	0
			Total	38	25	63	2
148 } 149 }	40	1910-July, 1913	*Antecedent Pellagra in Household*	..	..	..	..
			Jan., 1911-July, 1913	4	4	8	1
			Dec., 1912-July, 1913	2	5	7	1
			Mar., '13-July, 1913	4	0	4	0
			Feb., 1913-July, 1913	3	0	3	0
			Apr., 1913-July, 1913	2	2	4	0
			Mar., '13-July, 1913	2	0	2	0
			Apr., 1913-July, 1913	2	1	3	0
			Mar., '13-Apr., 1913	2	2	4	1
			1910-Feb., 1913	5	4	9	0
			Total	26	18	44	3
Total for this portion of the tab			.....	90	62	152	5

The result of this compilation of data in regard to location of domicile is very striking. Of the 819 non-pellagrin individuals who lived in the house in which pellagra existed at the time, 54 acquired the disease during 1912 and 1913. Of the 3,201 instances in which non-pellagrin individuals lived next door to a house in which pellagra was present, the disease developed in this exposed population in 55 instances during 1912 and 1913. Of the 3,105 persons who lived in houses farther away than next door to a pellagrin, 16 contracted the disease during the two years. The respective percentages are 6.59

TABLE 99.—Domicile Relationship, Village 1, Zone 3

Residence Period	Adults	Children	Total	Incident Pellagrins	Excluded from Zone 3 by Presence of Pellagra in Same or Adjacent House
Jan., 1913 - July, 1913	12	1	13	0	1911 to Aug., 1912.
May, 1911-July, 1913	3	2	5	0	1911 to Aug., 1912.
April, 1913-July, 1913	4	2	6	0	July, 12, '12, to Sept., 1912.
Nov., 1911-July, 1913	5	0	5	0	July, 12, '12, to Sept., 1912.
Oct., 1910 - July, 1913	2	1	3	0	July, 12, '12, to Sept., 1912.
Dec., 1911-July, 1913	2	1	3	0	1911 to March, 1912.
Feb., 1913 - July, 1913	2	2	4	0	1911 to March, 1912.
1909-July, 1913	2	3	5	0	1911 to March, 1912; July, 1912, to July, 1913.
Nov., 1911-Dec., 1912	2	1	3	0	.....
Jan., 1913 - July, 1913	2	4	6	0	.....
Jan., 1913 - May, 1913	2	1	3	0	.....
May, 1913 - July, 1913	2	1	3	0	.....
Apr., 1908 - July, 1913	2	0	2	0	June, 1912, to July, 1913.
Nov., 1909-July, 1913	3	4	7	2	July, 1912, to July, 1913.
Feb., 1910-July, 1913	4	0	4	0	1911 to March, 1912; June, 1912, to July, 1913.
Apr., 1908-July, 1913	2	1	3	0	1911 to March, 1912; June, 1912, to July, 1913.
Apr., 1911-July, 1913	5	0	5	0	June, 1912, to July, 1913.
Jan., 1912 - Jan. 1913	3	0	3	0	July, 1912, to July, 1913.
Nov., 1911-July, 1913	2	4	6	0	.....
Nov., 1911-Sept., 1912	2	4	6	0	.....
Apr., 1913 - July, 1913	2	1	3	0	.....
Total for this portion of the table	65	33	98	2	

for Zone 1, 1.72 for Zone 2 and 0.52 for Zone 3. As far as these mill villages are concerned it is clearly evident that a high degree of correlation existed between proximity of domicile to an existing case of pellagra and the origin of new cases in the population of such a domicile. In other words, the new cases of the disease developed almost exclusively in small foci, within which one or more old cases of the disease already existed.

The figures presented above have been subjected to a critical scrutiny with especial attention to the accuracy and the completeness

TABLE 100.—Incidence of Pellagra in the Population of Different Zones According to Location of Domicile in Relation to Domicile of an Antecedent Pellagrin .

Village	Zone 1			Zone 2			Zone 3		
	Instances of Exposure	Incident Pellagrins	Incidence Per Cent.	Instances of Exposure	Incident Pellagrins	Incidence Per Cent.	Instances of Exposure	Incident Pellagrins	Incidence Per Cent.
I	115	7	6.09	832	20	2.40	608	4	0.66
W	83	7	8.43	323	7	2.17	240	0	0.00
P	141	7	4.96	499	8	1.60	993	4	0.40
Sa	211	10	4.74	593	10	1.69	150	0	0.00
A	70	9	12.86	175	7	4.00	276	2	0.72
Sp	199	14	7.04	779	3	0.38	838	6	0.72
Total	819	54	6.59	3,201	55	1.72	3,105	16	0.52

of our records and to the possibility of association with other cases of pellagra besides the antecedent cases here considered. In regard to Zone 1, this scrutiny has shown a high degree of accuracy and completeness. In many instances the household in which an old case of pellagra existed had been examined and detailed record of it made previous to the development of the secondary cases. The development of new cases presented opportunity to verify and extend the records already made. In Zone 2, the cases have not, on the whole, been so completely studied and in some of these the location of previous residences is incompletely known and, in some instances, the possibility of close association with other pellagrins by visits is clearly indicated by the records. In Zone 3 there are only 16 incident cases and they will be considered briefly in order.

Patients 152 and 157, at village I, were father and son. They had been living in the same house for three years, during which time no patient with pellagra had resided in the immediate vicinity. The nearest case was at a distance of five houses, in the village. Both of these persons developed pellagra about the same time, in June, 1912. The father of the older patient, grandfather of the boy, is said to have pellagra. He lives at a distance of about a mile in the country. We have no further information in regard to him. The wife and mother in this family has been in poor health for some years, but there is no definite history and no evidence of pellagra in her. The two cases have been placed in Zone 3. As far as relation of domicile is concerned, one cannot be considered secondary to the other. A third case in village I is Patient 153, a little girl aged 5. Her family had lived in the village part of the time ever since her birth. During the spring and summer of 1911 they lived on a farm some distance from the village and moved to the present residence the last of November, 1911. The little girl suffered from diarrhea since early in the spring of 1912 and developed the erythema in March, 1912. We have not been able to obtain information concerning the associations at the farm. The case therefore falls in Zone 3. The fourth case in village I is Case 280, a woman aged 28, living in a house removed from cases of pellagra by one intervening house. Her father-in-law, Patient 316, died of pellagra in August, 1911, in the house next door but one from the house in which this patient was living. In Case 280, erythema developed for the first time in July, 1912. Evidence of living next door to a pellagrin is absent in this case and it is therefore placed in Zone 3.

In village W there are no cases in the third zone to be considered.

In village P there are four cases in Zone 3. Case 54 was in a boy aged 12, who developed pellagra for the first time in May, 1912.

He had lived in the same house in this village since March 6, 1912, having come from Lee County, Va. There was no recognized case of pellagra among the persons living in any of the adjacent houses at this time. In a house next door but one, there was a little girl who had suffered from pellagra for about a year. In the spring of 1912 three cases of pellagra in children originated in this immediate vicinity; one in the younger sister of this original case, one in a girl aged 10, who lived next door, and one in this boy we are now considering, Case 54. The three families lived in adjacent houses, the house in which the 10-year-old girl lived being between the house of the original case and this Case 54. These three children all developed pellagra about the same time and it is therefore impossible to regard the case of this boy as secondary to that in the girl living next door to him. He has been placed in the third zone. In Case 630, a girl aged 8, pellagra developed for the first time in July, 1912, while the patient was living in a house in Zone 3. Her mother, Patient 299, died of pellagra in June, 1911. The child lived with her mother in the same house in which the child developed the disease later. Her mother, however, was taken from this house shortly before she died, to her father's house, grandfather of Patient 630, a short distance away in the same village, where she died. The grandfather developed pellagra during 1911. The evidence of close association between the child, its mother and grandfather, is, of course, very clear; but inasmuch as the domicile in which the erythema developed is further away than next door from the grandfather's house and the mother was removed from this domicile about a year before the child developed the disease, the case is placed in Zone 3. Patient 640 was a woman aged 27 who had been living in the same house since 1910. She developed pellagra for the first time in June, 1913. The house is next door but one to a house containing two cases of the disease which developed in 1912. In the same house where this woman lived there was a boy, Patient 521, who had pellagra in the summer of 1911. He had lived in this house since 1908 and moved away in September, 1911. Patient 557 was, of course, associated with this boy in the same house during 1911, but inasmuch as the record shows that she developed her erythema in June, 1913, nearly two years after the other patient had left, she is placed in Zone 3. Patient 634 was a woman aged 35. She developed erythema for the first time the latter part of July, 1913. She had been living in the same house since February, 1912, and there was no case of pellagra within a radius of four houses. Previous to February, 1912, she had lived on the other side of the river near her father's house. The exact location of her residence there has not been ascertained. Her father, Patient 300, developed pellagra in 1911 and died of pellagra

in August, 1912. The evidence of association between these two cases has not been definitely ascertained, but even if it were fully known, the domicile in Case 634 would, nevertheless, remain in Zone 3. This woman died of pellagra, Sept. 23, 1913.

In village Sa we find no cases of pellagra which developed in houses at a greater distance than next door from a previous case.

In village A, two persons developed the erythema for the first time while living in houses which did not contain a case of pellagra and which were not adjacent to such houses. One of these, Patient 594, was a woman aged 30, who had lived in her present residence since October, 1912. She developed erythema for the first time in June, 1913. Her residence previous to October, 1912, had not been definitely ascertained. During the winter of 1912 and 1913, that is, from November, 1912, to January, 1913, Patient 570 lived in the same house. Patient 570 is believed to have developed erythema for the first time in June, 1913, after leaving this house, but her sister states that she had suffered from pellagra also during the summer of 1912. The exact information in regard to this point is lacking. As we do not know with certainty of any association in the household or of any next-door relationship to a previous case, we have placed Case 594 in the third zone.

Case 579 was in a boy aged 4. He had been living in his present residence since December, 1912, and developed erythema for the first time in June, 1913. During this interval, from December to June, there was no recognized case in the same house or in any of the adjacent houses, excepting one. In this one exceptional house, three cases of pellagra developed in 1913, one on May 1, one on June 19 and one on June 25. Two of these cases were in young children. In our study of relation of domicile we decided not to consider a case as a center of origin unless the patient had resided in this particular village previous to April, 1913. It is therefore impossible to include this case, 579, in our Zone 2. This child, however, played with the other children a large part of the time, and there is no question that association with other pellagrin children in the immediate neighborhood was very close.

In the village Sp there are six cases to consider. Patient 747 was a woman aged 44 who had been living in her present residence since 1907. She was observed to have pellagrous erythema in October, 1913. She refused to give us information concerning her history, except to say that she had been ailing for three years. There was no antecedent case of pellagra within a radius of four houses and, in the absence of more complete information, this case has been credited to Zone 3. Case 748 was in a woman aged 44, who was living directly across the

street from Case 747. She had been in this house since 1906. Erythema developed for the first time in August, 1913. This patient was also very reluctant in giving her history. It is perhaps justifiable to consider her as a case developed next door to Case 747, but in the absence of more complete information we have placed her in Zone 3. Patient 548, a girl aged 5, had been living in her present residence since September, 1913. The nearest antecedent case of pellagra was three doors away. The little girl developed erythema for the first time about June 1, 1913. Her parents both worked in the mill, and she played with the neighbors' children most of the time. We were unable to find that she actually lived in the house with a case of pellagra or in a house next door to such a case. Patient 718, a woman aged 42, had been living in her present residence since April, 1912, and she developed erythema for the first time in May, 1913. Her previous residence had been across the street from a case of pellagra. Her residence in 1913 was an apartment house in which there were no other cases of the disease. The association in the previous house was too remote to come within the limits which we have set for ourselves in this study. She has been placed, therefore, in Zone 3.

This brief examination of the cases originating in a house farther away than next door from an antecedent case of pellagra shows that in most of the instances there is evidence of previous close association with cases of pellagra or that our information is too incomplete to warrant a final opinion in regard to this question. It serves to strengthen rather than weaken the indication shown by the tabulated figures. We are forced to conclude that the origin of pellagra in persons living at a distance from previous cases of the disease in these particular mill villages was relatively very uncommon in 1912 and 1913.

DISCUSSION OF FOODS AND OF LOCATION OF DOMICILE AS ETIOLOGICAL FACTORS IN PELLAGRA

The preceding pages have presented the data concerning the use of particular foods and concerning the location of domicile in relation to pellagra, obtained by an intensive study of the inhabitants of six mill villages. It remains to discuss these facts presented and their bearing on the problem of the causation of pellagra.

In the first place the data do not support the theory that pellagra is an intoxication, the recurrent manifestations of which are due to the continued use of maize. The simple fact is that the portion of the population rarely or never using shipped corn contained a relative excess of pellagrins as compared with those using this food daily. Of those persons using shipped corn daily, 3.02 per cent. were pellagrins; of those using it habitually, 3.92 per cent., of those using it rarely or never, 5.49 per cent. The relation to local corn-meal was somewhat

similar. Of those persons using it daily, 2.99 per cent. were pellagrins; of those using it habitually, 3.90 per cent.; of those using it rarely or never, 3.83 per cent. The study of corn-meal, both kinds considered together, gave an even more emphatic result. Of those persons using it daily, 3.13 per cent. were pellagrins; of those using it habitually, 4.30, and of those using it rarely or never, 6.02 per cent. were pellagrins. It would seem justifiable to dismiss at once the idea that continued use of maize was the important factor in producing the symptoms of pellagra in the population of these villages.

A precisely similar conclusion may be drawn concerning the supposed toxic influence of canned foods as a primary factor in the causation of the symptoms of pellagra. Of the 89 persons using canned foods daily, none were pellagrins; of those using these foods habitually, 3.25 per cent. were pellagrins; of those using them rarely or never, 4.12 per cent. were pellagrins.

So far as we are aware, no one has yet ascribed the causation of pellagra to the use of fresh meat, milk or eggs, and we do not perceive any reason for giving them any consideration as direct causes of this disease.

In the second place it is necessary to examine the food data from the point of view of those who regard deficiency in total amount or in the quantity of particular elements of the food as the real cause of the symptoms and lesions of pellagra. The data presented in the preceding pages have little bearing on the theory that pellagra is the direct result of a general deficiency in diet. Our observation of pellagra in apparently well-nourished growing children, however, as well as in apparently well-nourished adults, have made this conception appear unworthy of consideration. The theory that a deficiency in some special dietary constituent may cause pellagra seems worthy of much more attention, especially because of the brilliant success attained in the prophylaxis of beriberi by measures based on a similar theory of causation in that disease. In general the dietary in these villages showed considerable variety. Most of the families possessed small gardens, and fresh vegetables were everywhere used in season. The data concerning the use of fresh meat, milk and eggs would appear to have a particular bearing on this question, because these foods might be supposed to contain the particular substance or substances, a lack of which would be assumed to cause the signs and symptoms of pellagra. Of the 82 persons in families using fresh meat daily, four were pellagrins, 4.88 per cent.; of the 2,591 persons in families using this food habitually, 3.74 per cent.; of the 2,460 persons in families using this food rarely or never, 3.98 per cent. were pellagrins. Most significant of all, perhaps, was the fact that of the 263 persons never

using fresh meat, only 4, or 1.52 per cent., were pellagrins, a figure considerably below the average morbidity for the whole population considered, namely, 3.88 per cent. Evidently the fresh meat used in these villages cannot be regarded as the essential pellagra-preventing food.

The data concerning the use of milk do show evidence of a relation of this food to pellagra. Of the 3,171 persons in families using milk daily, 89, or 2.81 per cent., were pellagrins, while of the 619 persons avoiding the use of milk, 43, or 6.95 per cent. were pellagrins. An analogous apparent effect of milk in preventing the development of new cases of pellagra was also evident in the study of the incident cases. We do not regard deficiency of milk in the diet as the cause of pellagra, however, because pellagra existed in many families in which milk was used daily and we have records of many cases of pellagra in persons who habitually drank sweet milk or buttermilk, and of several who drank buttermilk daily. Furthermore, it is well known that milk and milk products, although valuable dietary elements for adult man, are not absolutely essential for his nutrition. A further reason for refusing to accept deficiency in milk as the essential cause of pellagra is its complete failure to account for the focal distribution of the incident cases so clearly brought out in the domiciliary study. Nevertheless, as far as these data are concerned, milk, including buttermilk, stands out prominently as the one dietary element which seems to have had any influence at all on the prevention of pellagra, and the number of persons included in each of the groups using this food daily, habitually, rarely and never is sufficiently large to give some weight to the evidence.

The use of eggs exerted no apparent influence on the existence of pellagra and only an uncertain influence on the origin of new cases. The pellagra morbidity in the 170 persons avoiding the use of eggs was only 2.94 per cent., while the average for the total population considered in this relation was 3.67. Of the population considered in relation to the incidence of pellagra, 175 persons never used eggs. Of these, 6, or 3.43 per cent., contracted the disease, an incidence somewhat above the average, 2.10 per cent., for the total population considered. The small number of persons in this group (175), and the great irregularity of the figures in the different villages, render the average figure, 3.43 per cent., very unreliable as an indication of the value of eggs in preventing pellagra. We are inclined to ascribe no importance whatever to this article of diet.

The omission or restriction of the use of corn-meal does show a slight associated increase in pellagra. For example, the 123 persons who avoided the use of corn-meal altogether included 6 pellagrins,

a morbidity of 4.88 per cent., as against an average of 3.81 per cent. in the total population considered. Similarly, of the population considered in relation to incident cases, 123 persons avoided the use of corn-meal and four of these contracted pellagra, an incidence of 3.25 per cent., as against an incidence of 2.14 per cent. for the whole 5,056 persons considered. We do not believe that omission of maize from the diet has contributed essentially to the increase of pellagra. The real explanation seems to be that some of those persons who already had the disease have restricted their use of maize and in some cases other members of their families have done the same. As has been shown in the domiciliary study, those persons closely associated with preexisting cases of pellagra contracted the disease most frequently. The slightly higher incidence among those taking little or no corn-meal is probably to be explained, therefore, by a relatively closer association of these persons with previous cases of the disease; an association which tended to produce two results, namely, restriction in the use of corn-meal and also a higher incidence of pellagra.

In the third place we wish to consider the bearing of the facts presented on the theory that pellagra is an infectious disease. The relationships discovered in the domiciliary study seem to us to be conclusive evidence of the correctness of this view. It is evident that, so far as was observed in the population of these mill villages in 1912 and 1913, the location of one's domicile in the same house with, or next door to a pellagrin, or farther away, had a greater and more definite relation to the subsequent development of pellagra than did the use or avoidance of any of the foods to which attention has been given. The observations indicate very clearly that pellagra actually spread in these villages from a preexisting case as a center, and that it spread readily only within a very small area surrounding such a preexisting case.

In order to present in a graphic manner the apparent relation of these dietary elements and of location of domicile to the origin of new cases of pellagra we have constructed a series of charts to illustrate the data in regard to incident cases, showing by actual area of each column the number of persons in families using each of the foods daily, habitually and rarely (including never) in each of the mill villages. These charts (Figs. 3 to 26, inclusive) show at a glance the relative number of the population in each of the frequency groups in respect to each of the seven foods studied and, in a precisely similar way, the population in each of the three domiciliary zones in the same village. In each of the large columns a smaller black column at the lower left corner indicates the actual number of that group which contracted pellagra during 1912 and 1913. The variation in the size

of the different dietary and domiciliary groups in the different villages is shown very clearly.

Figure 28 shows the incidence of new cases per ten thousand in the total population in the six villages using each of the foods daily, habitually and rarely (including never). The *higher* incidence of pellagra in those who rarely or never used corn-meal, the *higher* incidence in those who did use fresh meat daily, the *absence* of incident cases among those using canned foods daily, and the *lower* incidence among

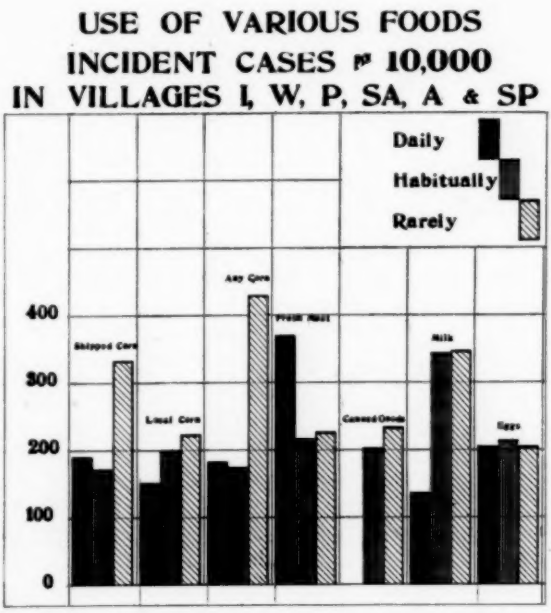


Fig. 28.—The incidence of new cases of pellagra in the total population of the six villages in each of the three groups summarized according to frequency of use of the various foods.

those using milk daily can be appreciated at a glance. It is, of course, necessary to refer to the preceding charts or to the tabulated data to ascertain the size of each group, in order to know the significance of the ratios shown here.

Figure 29 shows in a similar way the incidence rate per ten thousand in each of the three domiciliary zones for each of the six mill villages and, at the right under "Av.," for the total population considered together. This distribution of incident cases can be accounted for, in our opinion, only by the conception that pellagra is an infectious disease spreading from a preexisting case as a center. Further-

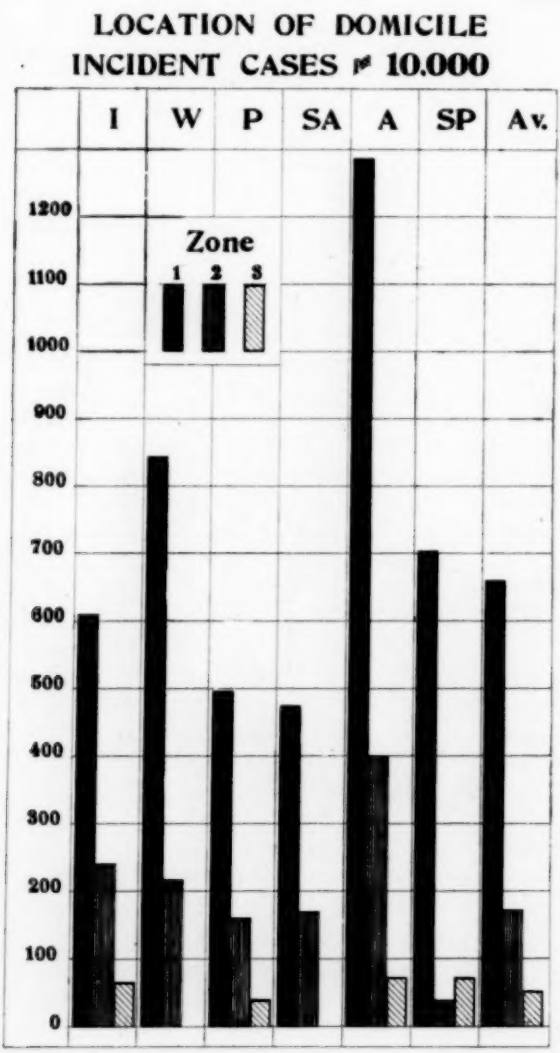


Fig. 29.—The black columns indicate the incidence of new cases of pellagra among persons living in the same house with a preexisting case. The columns striped vertically indicate the incidence in the population living next door. The columns striped obliquely indicate the incidence in the population living within the respective village, but farther away than next door from a preexisting case of pellagra.

more, it seems in general not to be very readily transmitted even to those in the same house, and its spread to those at a greater distance is very much less common. It should be remembered that nearly two years elapsed while the new cases on which this chart is based were originating.

Summary

1. Pellagra spread from a preexisting case as a center in the six villages here studied.

2. It was transmitted to new victims only through very short distances and chiefly to those immediately associated in the home with a preexisting case of the disease.

3. Frequent use of corn-meal as an article of diet was not a factor in the causation of pellagra in these villages.

4. There was discovered no evidence that canned goods have anything to do with the causation of pellagra.

5. Frequent use, even daily use, of fresh meats and of eggs afforded no relative protection from pellagra in these villages.

6. The daily use of milk seemed to diminish to some extent the danger of contracting pellagra in these mill villages in 1912 and 1913, although its use did not fully insure against the development of the disease.

NITROGEN AND SULPHUR METABOLISM IN A CRETIN *

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In spite of a number of observations on the balance of nitrogen, phosphorus, calcium and other elements in the metabolism of cretins, there appears to be only one series of experiments on record in which careful determinations of the amounts of the various nitrogenous constituents of the urine were made. These were reported by Scholz[1] in 1906. According to him, the nitrogen partition is practically normal. Unfortunately, of the methods then available, only those for the deter-

NITROGEN AND SULPHUR METABOLISM—

Date Jan., 1913	Nitrogen in Food, gm.	Nitrogen Excretion in Gm.					
		Total	Urea	Ammonia	Creatinin	Creatin	Uric Acid
8	5.38	3.998	3.053	0.163	0.0550	0.0115	.....
9	5.38	2.440	2.300		0.0339	0.0137	.....
11-13	4.27*	3.000	2.520	0.248	0.0470	0.0120	0.0408
19-20	5.22*	3.150	2.394	0.347	0.0450	0.0260	0.4000
21-22	5.60*	3.634	3.144	0.287	0.0579	0.0185	0.0438

* In the last three periods the figures are for twenty-four hours.

mination of nitrogen, urea and ammonia can be considered at all reliable. More recently, McCrudden[9] studied the excretion of creatinin and creatin in a cretin. The amount of creatin eliminated was much less than in other types of arrested development and was greater on a carbohydrate-rich diet than on one rich in fat. The sulphur metabolism of cretins has, apparently, never been studied.

An opportunity to study the metabolism in a cretin girl presented itself and it was considered advisable to pay particular attention to the distribution of nitrogen and sulphur in the urine.

* Submitted for publication Nov. 17, 1913.
* From the Chemical Laboratory of the Montefiore Home.
1. Scholz: Ztschr. f. exper. Path. u. Therap., 1906, ii, 271.

Examination of the results show few deviations from the normal. The absorption of nitrogen is poor. The ratio of ammonia-nitrogen to total nitrogen is rather high. The creatinin output is very low, much less than in McCrudden's[9] case and a considerably greater amount of creatin is excreted. Aside from these the findings seem to be quite normal.

The patient, A. S., aged 7, weighed 15.5 kg. (34 pounds). Her general behavior was that of a sluggish child of 8 or 9 months. The thyroid was not palpable, and in every way she presented the picture of a typical cretin.

The girl was placed on a diet consisting of farina, oatmeal, milk, toast, butter and eggs, and an attempt was made to collect the urine and feces separately. Various devices were used, but none were satisfactory. It was noted, however, that defecation occurred only once in three or four days. This made the collection of urine free from feces rather easy. A bed such as that described by Du Bois[2] was used. A trough of galvanized iron was arranged so as to collect all the urine and conduct it into a bottle containing thymol.

—IN CASE OF A. S., A CRETIN

Sulphur Excretion in Gm.			Percentage of Total Nitrogen as					Percentage of Total Sulphur as	
Total	Total SO_4	Inorg. SO_4	Urea	Ammonia	Creatinin	Creatin	Uric Acid	Sulphate	Inorganic Sulphate
.....	.....	.....	89.87	4.78	1.62	0.34	....	....	....
0.205	0.192	0.184	94.26		1.39	0.56	....	93.5	89.8
0.259	0.240	0.231	84.05	8.27	1.56	0.42	1.36	92.6	89.0
0.273	0.253	0.245	76.09	11.01	1.42	0.92	1.26	92.8	90.0
0.290	0.256	0.241	86.49	7.91	1.59	0.51	1.21	88.5	75.9

This trough was washed with distilled water every day and the washings were added to the urine. If defecation occurred, the urine was not used. When the urines of two or more days were combined, the earlier specimens were kept in a refrigerator until the later urines were obtained. The following methods were used: Total nitrogen, Kjehldahl-Gunning; urea, Benedict;[3] ammonia, Folin;[4] creatinin and creatin, Folin;[5] uric acid, Folin-Shaffer;[6] total sulphur, Benedict;[7] inorganic and total sulphate, Folin.[8] The nitrogen of the food was calculated according to the data given in Bull. 28, U. S. Dept. Agric.

2. Du Bois: Am. Jour. Dis. Chil., 1911, ii, 419.
3. Benedict: Jour. Biol. Chem., 1910, viii, 405.
4. Folin: Ztschr. f. physiol. Chem., 1902, xxxvii, 161.
5. Folin: Ztschr. f. physiol. Chem., 1904, xli, 222.
6. Folin and Shaffer: Ztschr. f. physiol. Chem., 1900, xxxii, 552.
7. Benedict: Jour. Biol. Chem., 1909, vi, 363.
8. Folin: Jour. Biol. Chem., 1906, i, 131.

LYMPHOCYTE INCREASE AND ALTITUDE*

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During the past few years much accurate and careful work has been done to establish the exact influence of altitude on the blood. The accumulated evidence would seem to have settled the fact that there is a definite increase in the number of erythrocytes and in the content of hemoglobin. At a moderate altitude of about 6,000 feet this increase is at least 10 per cent. in both instances. No increase in the total number of leukocytes has been found. Little attention was paid to the differential blood-count at various altitudes until recent years.

In April 1909, Webb and Williams[1] first called attention to an absolute increase in the lymphocyte or mononuclear element of the blood as an effect of altitude. In this and the previous year evidence regarding the defensive behavior of the lymphocytes in tuberculosis had been brought forward, notably by Bartel,[2] Bergel[3] and Marie and Fiessinger.[4] The latter demonstrated that lymphocytes contain a lipolytic ferment which can destroy the waxy coat of the tubercle bacillus. These connected observations suggest a partial explanation of the apparently low incidence of tuberculosis among the inhabitants of high altitudes and also of the reputed curative virtues for the tuberculous of mountain resorts.

Stäubli,[5] in 1910, published a few figures which showed an increase in the lymphocytes at a high altitude. Quite recently Baer and Engelsman[6] of Davos, have thoroughly corroborated this observation.

* Submitted for publication, March 14, 1914.

* From the Laboratory of Cragmor Sanatorium, Colorado Springs, Colo.

1. Webb and Williams: Some Immunity Problems in Tuberculosis, Colorado Med., April, 1909; Some Hematological Studies in Tuberculosis, Tr. Nat. Assn. for the Study and Prevention of Tuberculosis, 1909.

2. Bartel: Experiments in Immunization Against Tuberculosis, International Congress on Tuberculosis, 1908.

3. Bergel: Fat-Splitting Ferment in Lymphocytes, München. med. Wchnschr., 1909, No. 2, p. 64.

4. Marie and Fiessinger: Compt. rend. Soc. de biol., July 23, 1909.

5. Stäubli: Beiträge zur Kenntnis des Einflusses des Hochgebirgsklimas, Verhandl. d. deutsch. Cong. f. inn. Med., 1910.

6. Baer and Engelsmann: Das Leukocytenbild bei Gesunden und Lungentuberkulosen in Hochgebirge, Deutsch. Archiv. f. klin. Med., 1913, cxii.

O. M. Gilbert[7] also confirmed the work of Webb and Williams by finding greater percentages of lymphocytes in specimens of blood taken at an altitude than in specimens taken at sea-level, although below sea-level he observed even higher counts. Too few and too incomplete observations, however, were made to be of marked significance.

During the year 1911, when discussing the present attitude toward climate, Dr. E. R. Baldwin[8] of Saranac Lake, wrote:

> If Dr. Webb's observations about the effect of altitude should be confirmed, I think it would be an important element in the matter of the treatment of tuberculosis. So far I have not heard of any confirmation nor any control experiments on a large scale which would make assertions very safe yet. I hope that he and his associates will continue to study it and give us some facts about it.

Realizing the importance of these remarks, we have continued to study at every opportunity the influence of altitude on the differential blood-picture and slowly and carefully to collect scientific data on this question.

During the summer of 1911 blood-films were obtained from the members of the Anglo-American Physiological Expedition[9] to Pike's Peak during their six weeks' residence at an altitude of 14,000 feet. These specimens exhibited a very marked increase in the percentage of lymphocytes.

This paper will report a series of differential leukocyte counts on 100 male students at Cornell Medical College in New York City, and on 100 male students at Colorado College in Colorado Springs. Each student was ascertained to be in normal health and between the age of 20 and 30. All counts were taken at twelve noon before lunch and when no strenuous exercise had been taken during the morning. The technic used in New York was identical with that used in Colorado, every detail having been previously arranged. The first blood was wiped away and the specimen was taken from a free flowing drop either from finger or ear. As thin a film as possible was obtained on a pair of cover-slips. Hastings' and Wright's stains were used interchangeably. In every instance at least 200 cells were counted and more often 300. A total leukocyte count was made at the same time.

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7. Gilbert, O. M.: Differential Leukocytes at Various Altitudes, Colorado Med., December, 1911.

8. Baldwin, E. R.: Quoted by A. M. Forster. The Present Attitude Toward Climate, Tr. Seventh Annual Meeting Nat. Assn. for the Study and Prevention of Tuberculosis, p. 230.

9. Webb: Phil. Tr. Roy. Soc. London, Series B, Vol. ccv, p. 312. Studies in Tuberculosis, Johns Hopkins Hosp. Bull., August, 1912.

In 156 cases a red count was also made as indicated. Nearly all the films taken in New York were recounted in this laboratory. The counting extended over a period of several months during the year 1913.

Table 1 presents a summary of the results of this work. It will be noted that we group all the basophilic mononuclear cells together and make no attempt to classify them according to origin, function or fate. Whether the transitional cells should be grouped with the large mononuclear cells is, of course, a much-disputed question.

TABLE 1.—Differential Leukocyte Counts on One Hundred New York Students and One Hundred Colorado Students

	New York Students*	Colorado Students	Percentage Increase
Mononuclear Percentages—			
Average	*34.4 (35.3)	42.8	24 (21)
Mean	34.0 (34.0)	42.5	
Extremes	27.0-45	26.5-60	
Total Mononuclears per cm.—			
Average	2,522	3,279	30
Mean	2,450	3,172	
Extremes	1,320-4,300	2,268-5,332	
Polymorphonuclear Percentages—			
*Average	62.3	55.0	
Extremes	52.0-70	35.0-73	
Erythrocytes—			
Average	4,875,920	5,984,000	22
Mean	4,864,000	5,952,000	
Extremes.	4,416,000 to 5,480,000	5,156,000 to 7,216,000	
Total Leukocytes—			
Average	7,340	7,795	
Mean	7,000	7,440	6

*Most of these slides were recounted in Colorado and the average was found to be 35.3 per cent., the mean 34 per cent. This shows a close comparison in the counting in New York and Colorado in regard to the total mononuclear elements.

The blood-counts were made in New York by Dr. Carolyn Rosenberg under the direction of Dr. T. W. Hastings of the Cornell Medical School.

The figures in Table 2 illustrate the manner in which the cells were divided and are taken from persons representing about the mean.

The work above reported shows an increase of 22 per cent. in mononuclear cells and of 22 per cent. in red blood-corpuscles at this altitude over the same components at sea-level.

The increase of 6 per cent. in the total white blood-cells at this altitude may be without significance, yet it may possibly prove to be a new observation. For many years it has been known that a temporary leukocytosis occurs in the blood of persons arriving at a high altitude.

The attempt was made to differentiate the smallest lymphocyte cells with very scant protoplasm surrounding the nucleus, from the larger ones with more abundant protoplasm.

These distinctions, however, seemed to vary according to the thinness with which the films were spread, and the larger lymphocytes could not easily be distinguished from the smaller, when the

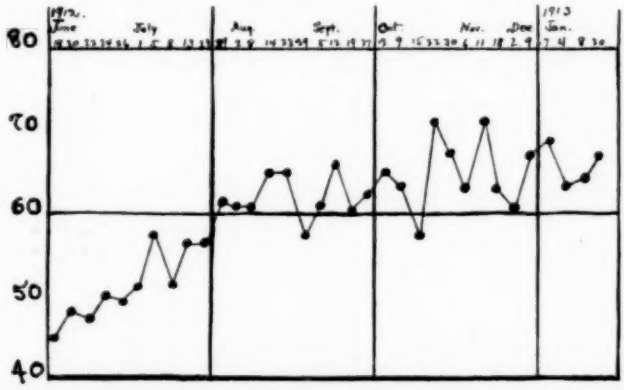

Chart 1.—Composite curve of the differential leukocyte count in twelve healthy *Macacus rhesus* monkeys brought from New York City to Colorado Springs, June 17, 1912. The counts of a monkey which broke its leg July 1 are omitted after that date; the counts of another in which tuberculosis was proved October 2 are not included after that date.

smears were not exceedingly thin. The figures indicate, however, that these distinctions were attempted, and they seem to prove that it is the larger lymphocytes of the mononuclear elements that are increased at this altitude.

On June 17, 1912, the arrival of twelve healthy *Macacus rhesus* monkeys from New York City gave us further opportunity for an accurate observation of the possible influence of the change in altitude on the differential leukocyte picture. Films were taken from all monkeys every few days for a period of several months. The blood was obtained from the ear vein at noon when the animals were fasting. The total leukocyte count remained practically stationary during this period.

TABLE 2.—Distribution of Cells in Persons Representing About the Mean

	Polymorphonuclears	Very Small Lymphocytes	Larger Lymphocytes	Large Mononuclears	Transitionals	Total Pct. Mononuclear Element	Eosinophils	Mast	Total Leukocytes per c.mm.	Total Mononuclears per c.mm.
New York	63.0	22	3	5.0	4.0	(34)	2⅔	⅓	7,000	2,380
Colorado Springs..	54.5	7	29	1.5	5.5	(43)	2.5	0	7,390	3,169

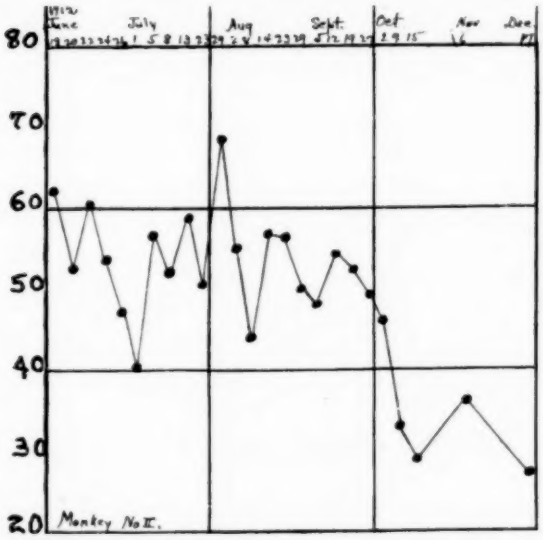

Chart 2.—Percentage of change in the mononuclear elements in a tuberculous monkey.

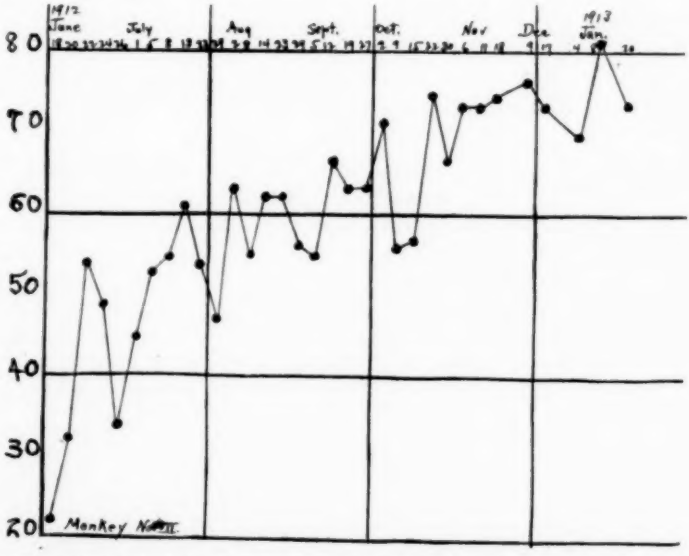

Chart 3.—Typical rise in the percentage of lymphocytes of a normal monkey.

Chart 1 is a composite showing the average percentage of mononuclear cells on the dates given. The increase from about 50 per cent. to 65 per cent. shows a percentage increase of thirty, and represents a very definite rise in the total numbers.

The counts on Monkey 4 are not included in this average after July 1, on account of its leg having been broken. The counts on Monkey 2 are also not included after October 2 when tuberculosis was suspected and confirmed.

Chart 2 illustrates the percentage of change in the mononuclear elements resulting from tuberculous infection in this monkey. The probability is that this monkey was infected on arrival, although the tuberculin test at that time was negative. Oct. 14, 1912, after the large decrease in the percentage of lymphocytes was noticed, a tuberculin test was found to be positive. The animal was killed Jan. 29, 1913 and showed extensive tuberculosis.

Chart 3 delineates the typical rise in the percentage of lymphocytes of a normal monkey.

CONCLUSIONS

1. It is certainly safe to assert that at an elevation of 6,000 feet the larger lymphocytes are absolutely increased in the circulating blood by at least 20 or 30 per cent. in both man and monkey.

2. The basophilic mononuclear elements in the blood of man at sea-level are approximately 34 per cent., and at 6,000 feet are about 42 per cent.

3. The total white blood-cells per cubic millimeter are approximately the same at sea-level and at an altitude of 6,000 feet, namely, about 7,500.

4. The total polymorphonuclear cells diminish in the exact proportion in which the mononuclear cells increase.

5. The red corpuscles increase by 22 per cent. at an altitude of 6,000 feet.

Our thanks are due to Dr. G. Burton Gilbert and Dr. T. W. Hastings for their kind supervision of this work.

This work has been aided by a grant from the American Medical Association to Dr. Gerald B. Webb. The authors are also under obligations to Mr. and Mrs. B. C. Allen and Mr. Richard F. Howe of Colorado Springs for their generous support.

THE GLYCYL-TRYPTOPHAN REACTION IN MENINGITIS *

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The presence of a proteolytic ferment in certain pathological exudates has long been known, and an examination of the literature discloses numerous investigations on the subject. Among these may be mentioned the work of E. Müller,[1] who, by the use of serum plates, showed the marked proteolytic action of pus cells. In the course of his investigations he also studied various exudates and transudates and found that normal cerebrospinal fluid contained no proteolytic ferment. In the cerebrospinal fluid of purulent meningitis he demonstrated the presence of ferment which digested the serum plates; in tuberculous meningitis no digestion occurred.

More recently Lenk and Pollak[2] have found the presence of a proteolytic ferment in certain exudates and transudates. They used glycyl-tryptophan as an indicator for determining the presence or absence of such a ferment. Glycyl-tryptophan, as is well known, first came into prominence through the publications of Neubauer and Fischer[3] who, following the work of Emerson,[4] which showed the presence of a proteolytic ferment in the gastric juice in carcinoma of the stomach, suggested it as a method of diagnosis. Subsequent investigations, however, especially those of Warfield[5] have shown the unreliability of this test. Warfield showed that sputum was able to split up the glycyl-tryptophan, and in addition to this peptid-splitting power of the sputum previous studies had already demonstrated the similar action of blood and bile.

Lenk and Pollak were especially impressed by the strong proteolytic or peptid-splitting powers of the cerebrospinal fluid in cases of tuberculous meningitis. In the normal cerebrospinal fluid they occasionally found such a ferment present in small amounts, whereas in tuberculous meningitis they found it present in large quantities and the fluid was usually able in dilutions of 1 to 100 or 1 to 200 to split the glycyl-tryptophan. In epidemic meningitis there was also a

* Submitted for publication May 9, 1914.
* From the K. K. Kinderklinik, Vienna.

1. Müller: quoted by Lenk and Pollak (Note 2).
2. Lenk and Pollak: Deutsch. Arch. f. klin. Med., 1913, cix, 350.
3. Neubauer and Fischer: Deutsch. Arch. f. klin. Med., 1909, xcvii, 499.
4. Emerson: Deutsch. Arch. f. klin. Med., 1901, lxxii, 415.
5. Warfield: Johns Hopkins Hosp. Bull. 1911, xxii, 150.

marked increase in the amount of the ferment, but dilutions higher than 1 to 10 or 1 to 20 failed to show any peptid-splitting action. In meningismus, often simulating true meningitis, they found no increase. Their material includes 8 cases of tuberculous meningitis, 5 cases of epidemic meningitis and 7 cases of meningismus.

Koch,[6] in a more recent publication, did not find the high values described by Lenk and Pollak, but in 7 cases of tuberculous meningitis found the reaction positive in the undiluted cerebrospinal fluid of all, although in 1 case only, was a dilution as high as 1 to 10 positive.

Mandelbaum,[7] working with cerebrospinal fluid obtained from cadavers, has confirmed the peptid-splitting powers in cases of tuberculous meningitis and reports some high dilutions of the cerebrospinal fluid having this power.

The advantages of glycyl-tryptophan in studying the peptolytic action of various exudates and transudates are quite obvious. It is a fairly stable polypeptid, but under the action of peptolytic ferments, tryptophan is split off whose presence is easily recognized. By acidifying slightly the solution to be tested and then adding a few drops of chlorin water or bromin water, a red color-reaction is obtained with tryptophan.

We were able during the winter of 1912-13 at the time of Lenk and Pollak's preliminary communication, to test out the reaction on the cerebrospinal fluid in 17 cases of meningitis and in 12 cases of other diseases in which a complicating meningitis was suspected. The results of these tests are given in the accompanying tables.

We were not so much interested in the question as to whether the glycyl-tryptophan test allowed the conclusion that the fluid examined was a transudate or an exudate, nor were we attempting to solve the question of the suspected fluid being tuberculous or non-tuberculous. Our primary object was to determine whether this test, so simple of application, was of practical value in making a probable diagnosis possible in certain obscure cases with meningeal symptoms. Also to see if this test aided us in clinching the diagnosis of an already fairly certain meningitis.

The carrying out of the test is quite simple. One cubic centimeter of the cerebrospinal fluid to be examined is placed in a test-tube with an equal part of glycyl-tryptophan and then 1 c.c. of toluol added as a preservative. In order to test the peptolytic powers of the cerebrospinal fluid, various dilutions with sterile normal salt solution up to 1 to 200 are made. The mixture is placed in the thermostat for three hours. At the end of that time it is withdrawn, a few drops of dilute acetic acid added, and then very carefully a small amount of over-

6. Koch: Ztschr. f. Kinderh. 1914, x, 1.
7. Mandelbaum: München. med. Wchnschr., 1914, lxi, 461.

saturated calcium chlorid which is briskly shaken just before using to give off free chlorin. It is safer to dilute the calcium chlorid 1 to 10 and it should be added drop by drop, as an excess of the solution masks the reaction. In the presence of free tryptophan a red color, as already stated, is found. Cerebrospinal fluid containing blood is of course to be rejected.

Here follow the tables of the cases in which these tests were applied. In these tables the highest dilution which was positive at any time is recorded, and the dilutions are indicated by the numbers set down, thus 10, 20, 50, refer to a dilution of 1:10, 1:20 and 1:50, respectively. The term "peptolytic index" which is subsequently used, refers to the dilution of cerebrospinal fluid which gave a positive reaction, thus "index 1" means undiluted fluid, "index 10" means a dilution of 1:10.

TABLE 1.—CASES OF MENINGITIS

No.	Age, Years	Clinical Diagnosis	Autopsy Findings	Positive Reaction	Negative Reaction			
1	2	Tub. men.	Tub. men.	20			50	100
2	2	Tub. men.	Tub. men.	200				
3	2	Tub. men.	Tub. men.	100				
4	8/12	Tub. men.	Tub. men.	100				
5	2	Measles, tuberculous meningitis	Tub. men.	5	10	20	50	100
6	1 8/12	Tub. men.	Tub. men.	50				
7	10	Tub. men.	Tub. men.	20	50	100	200	
8	2	Tub. men.	Tub. men.	50				
9	6	Tub. men.	Tub. men.	20	50	100		
10	1 1/12	Tub. men.						
11	2 1/2	Tub. men.	Tub. men.	1	10	20	50	100
12	7	Tub. men.	No autopsy	20				
13	4	Tub. men.	No autopsy	100				
14	4	Tub. men.	No autopsy	100				
15	1	Tub. men.	No autopsy	10	..	20		
16	5 1/2	Tub. men.	No autopsy	10	20	50		
17	1 1/2	Purulent meningitis (pneumococcus)	Purulent meningitis	1	10	20	50	100

TABLE 2.—NON-MENINGEAL CONDITION

No.	Age, Years	Clinical Diagnosis	Autopsy Findings	Positive Reactions	Negative Reactions				
1	9	Coma, meningitis?	Recovered	0	1	10	20	50	100
2	3½	Delirium meningitis?	Enteritis	0	1	10	20	50	100
3	7	Scrofula, coma, meningitis?	Brain abscess	0	1	10	20	100	
4	1½	Ant. poliomyelitis	Recovered	0	1	10	20	100	
5	2	Measles, miliary tuberculosis?	Recovered	0	1	10	20	50	100
6	12	Typhoid meningitis?	Recovered	0	1	5	10		
7	7*	Miliary tuberculosis	No autopsy	0	1	10	20	50	100
8	4	Measles, miliary tuberculosis?	Recovered	0	1	5			
9	4	Measles, miliary tuberculosis?	Recovered	0	1	5			
10	4	Scarlet fever	Recovered	0	1	10			
11	7	Scarlet fever	Recovered	0	1	5	10		
12	11/12	Hydrocephalus luetica	.....	0	1	10	20	50	100

* Weeks.

It will be seen on glancing over Table 1 that while tuberculous meningitis usually gave a positive reaction in high dilutions, yet this was by no means always the case. In Case 11 dilutions of the cerebrospinal fluid contained no demonstrable peptolytic ferment; in Case 5, 1:5 was the highest dilution positive and in Cases 10, 15 and 16 dilutions higher than 1:10 were negative. There is, however, evidence in our series of cases that this proteolytic index may vary from time to time. Cases 3, 6, 9, 11, 14 and 16 showed these variations. Case 6 is a good example.

CASE 6.—A. W. L., aged 20 months, male, admitted to hospital Feb. 21, 1913, with fever, rigidity of neck, stupor and unconsciousness. Clinical Diagnosis: Tuberculous meningitis.

The cerebrospinal fluid when tested for peptolytic ferment gave the following results in the various dilutions:

February 21—1+ 10 neg. 20 neg.
February 25—1+ 5+ 10+ 20 neg.
February 26—10 neg. 20 neg. 50 neg.
March 3—1+ 10 neg. 20 neg.
March 9—1+ 10+ 20+ 50+
Child died March 9. Anatomical Diagnosis: Meningitis tuberculosa.

Several cases have shown a gradually increasing peptid-splitting power of the cerebrospinal fluid as the disease progressed. Cases 1, 2, 4 and 8 exhibited this. Case 2 is a good example.

CASE 2.—O. F., aged 2 years, male, was admitted to hospital Oct. 26, 1912, with fever, unconsciousness, strabismus and rigidity of neck. Clinical Diagnosis: Tuberculous meningitis. Tests with the cerebrospinal fluid gave the following results:

October 26—1+ 20+ 40 neg. 100 neg.
October 29—1+ 20+ 50+ 100 neg.
November 2—1+ 10+ 50+ 100+
November 3—50+ 100+ 200+
Death on November 3. Anatomical Diagnosis: Meningitis tuberculosa.

In several cases the reaction was of distinct value in clearing up an obscure diagnosis. Case 4 is an example.

CASE 4.—L. K., aged 7, male, was admitted to hospital Oct. 30, 1912. Scrofulous child, Pirquet +. Coma, slow respirations, rigidity of neck. Cerebrospinal fluid showed no splitting of glycyl-tryptophan. Child died on day of admission. Anatomical Diagnosis: Brain abscess.

In none of the cases without meningitis was any splitting of the glycyl-tryptophan observed. Koch[8] reports one case of pneumonia with meningeal symptoms, and one case of sarcoma of the skull which gave positive reactions with undiluted cerebrospinal fluid. As the autopsy findings are not reported one is left in doubt as to whether there was an accompanying meningitis. Lenk and Pollak report several cases of meningismus in which positive reactions were found. In these cases autopsy showed the meninges to be free. From their

series of cases it seems probable that the undiluted cerebrospinal fluid in non-meningeal conditions may sometimes split glycyl-tryptophan. The study of a large series of normal cerebrospinal fluids would be desirable in order to settle this point definitely.

Far-reaching conclusions we do not wish to draw from the results in our cases. But we do feel that in glycyl-tryptophan we have another valuable addition to our diagnostic measures in meningitis. In cases having a peptolytic index higher than 1 we have consistently found meningitis present. Only one case of tuberculous meningitis showed an index as low as 1. The striking variations in peptolytic powers which were observed from time to time makes it probable that cases showing a low index might at some time have shown a much higher one. Also there was noted an interesting tendency for the peptolytic powers of the cerebrospinal fluid to increase as the disease progressed.

ELLIPTICAL HUMAN ERYTHROCYTES*

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The following observations are published in view of the rarity of the condition, and because of the interesting discussion which followed the report of the only other case on record.

April 14, 1913, J. F., male, aged 41, was admitted to the surgical service of Dr. Henry H. M. Lyle at St. Luke's Hospital, New York City, with the diagnosis of acute suppurative appendicitis. According to the routine procedure of the hospital a leukocyte count was made. While examining a stained smear to determine the differential count I noticed that many of the red blood-cells were not circular but elliptical. So striking was this poikilocytosis that in spite of the absence of erythroblasts, a diagnosis of pernicious anemia seemed to be warranted. An estimation of the hemoglobin, however, showed 110 per cent. (Fleischl-Miescher), and of the red blood-cells, 5,400,000.

The patient gave a typical history of acute appendicitis. No lesions of heart, kidneys or lungs were discoverable. Examination of his abdomen revealed tenderness and rigidity of the right lower quadrant. His temperature was 102 F., his leukocytes were 16,500, polynuclears, 82, lymphocytes, 18. Urine, acid, turbid, 1.015, albumin very faint trace, sugar, 0, few leukocytes. Operation was performed two hours after the patient entered the hospital and a gangrenous appendix with a small amount of seropurulent fluid free in the abdomen, was found. Recovery was uneventful, the temperature being normal on the seventh day after operation and the patient being discharged cured on the tenth day.

During his stay in the hospital a careful study of his blood was conducted. About 75 to 80 per cent. of the erythrocytes were observed to be elliptical in outline. The proportion between the long and short diameters of these cells varied considerably, some of them being only slightly elliptical, while others were very distinctly elongated. The following measurements may be interesting:

Circular cells measured 8.5 microns in diameter.
Greatest length observed, 13.7 microns.
Shortest length observed, 8.2 microns.
Shortest width observed, 5.0 microns.
Greatest width observed, 8.0 microns.
Most of the elliptical cells measured about 13.0 by 5.0 microns.

*Submitted for publication, April 27, 1914.

*From the Pathological Laboratory of St. Luke's Hospital, New York, Prof. Francis Wood, director.

Every precaution was taken to exclude the possibility of mechanical distortion of the cells. Smears were made by several persons, and by several methods, and the slides were dried both slowly and rapidly, but the deformity always appeared the same. Blood diluted with Hayem's solution also showed the anomaly; and finally specimens of the fresh blood were examined and the cells were still found to be elliptical.

The fragility of the erythrocytes was determined and found normal. Vital staining showed only 3 per cent. reticulated cells—well within normal limits. The Wassermann reaction was negative.

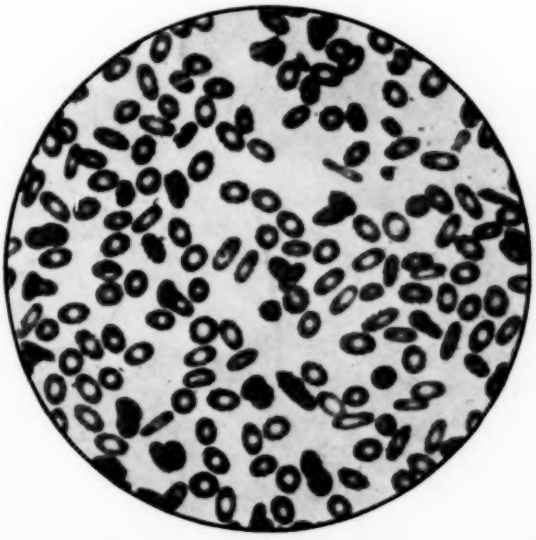

Fig. 1.—Blood from J. F., April, 1913, magnified 500 diameters, showing elliptical corpuscles. This and the Figures 2, 3 and 4 were all taken without changing lenses or apparatus, so that they are exactly the same magnification. The smears were made in the same manner.

The possibility of this condition being a congenital characteristic of the man's blood suggested itself. Working on this theory the blood of his sister was obtained and was found to show an exactly similar condition. Her red blood-cells were 5,000,000, her hemoglobin 100 per cent., and about 70 to 80 per cent. of her cells showed a more or less well-marked elliptical outline. A few of them showed a more extreme deformity than those of her brother. One cell was found to measure 17.2 by 3.2, and several were 15 microns long. As far as she could remember she had never had a sick day in her life.

The other members of the family—a second sister, her father and her two children (both boys)—were found to have normal erythrocytes; unfortunately the mother of my patient is not living. To exclude the possibility of some chronic poisoning by lead, coal-gas, or other chemical, the blood of all the persons living in the same house with this family was examined and found to be normal.

Mr. F. has been under observation for eight months and is apparently in perfect health, never having had any illness before or since his appendicitis. His blood has been examined six times during this period and has always shown the same unvarying deformity of the

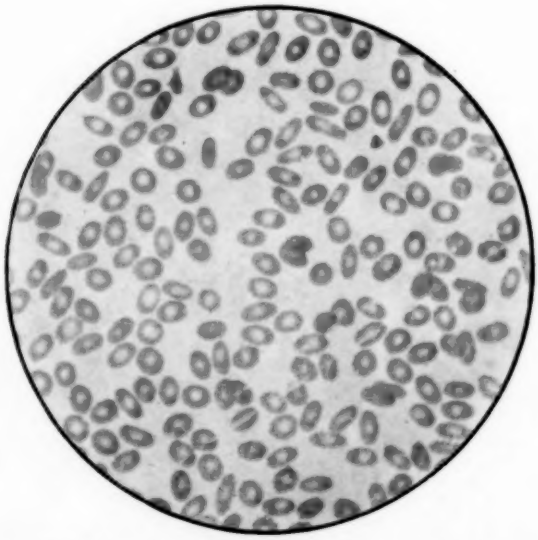

Fig. 2.—Blood from J. F., December, 1913, magnified 500 diameters.

red cells. His hemoglobin and the number of his red cells have always been normal. The same facts are true of the sister's blood.

The only record of a similar case which I have been able to find was that observed by Dr. Melvin Dresbach.[1] Dr. Dresbach reports that in 1902 a student working in the Ohio State University laboratory of histology discovered that his erythrocytes were elliptical in outline, 90 per cent. of the cells being deformed. Variously prepared and stained specimens and fresh blood were examined. His hemoglobin and the number of his red cells were normal. The case was studied over a period of four months and always showed the same

1. Dresbach, Melvin: Science, 1904, xix, and 1905, xxi.

characteristic. The following are the measurements given for this man's blood:

Shortest width observed	3.9 microns
Greatest width	4.8 microns
Shortest length	8.5 microns
Greatest length	10.7 microns
Average length	10.3 microns
Average width	4.1 microns

I have examined a photomicrograph of this blood and the picture is much the same as in J. F., but the amount of deformity is slightly greater.

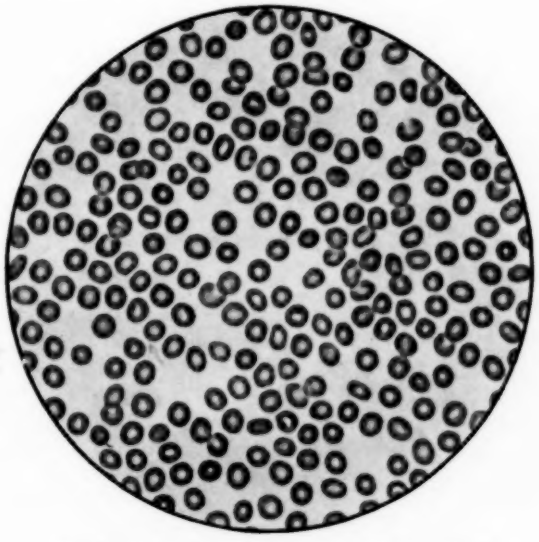

Fig. 3.—Normal blood magnified 500 diameters.

The student was a healthy mulatto, aged 22 years. Dr. Dresbach says:

The observation attracted considerable attention, Prof. Austin Flint being one among several who wrote to me for a specimen of the blood. There resulted some correspondence between Professor Flint and myself, and in a letter to him I remarked that some time after my observations had been made the young man having these elliptical corpuscles died. Since the claim had been made that the young man was healthy when these corpuscles were discovered, the statement about his death naturally aroused some suspicion. Professor Flint wrote a note which was printed in *Science*, May 20, 1904, discussing the matter of form changes in erythrocytes and pointing out that in progressive pernicious anemia and other blood diseases, variations in form and size are well known facts. He adds that in view of these facts it seems impossible to accept the proposition that the subject of the observation was a healthy mulatto. The cause of death was cardiac failure subsequent to an attack of

acute inflammatory rheumatism. The attack was preceded by tonsillitis, which began about three months after the time observations were made.

Prof. James Ewing of the Cornell Medical School, saw the blood specimen and was of the opinion that the anomaly was one of congenital or developmental origin—because the hemoglobin and number of red cells was normal and the patient's general condition good.

The slides were also shown to Prof. Paul Ehrlich, who thought that these cells showed a congenital anomaly. Dr. Dresbach gives the following reason for agreeing with these opinions, and I think they apply equally to my cases.

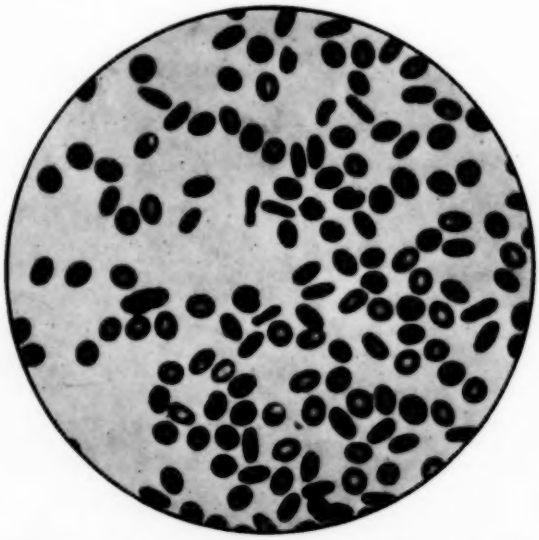

Fig. 4.—Blood from a sister of J. F., December, 1913, magnified 500 diameters.

The variation occurred in a healthy individual. Good general physical condition, normal number of red and white cells, normal hemoglobin and absence of normoblasts or megaloblasts preclude the idea of any known blood disease being connected with the phenomenon. In Dr. Dresbach's case no family history could be obtained except that a brother of the patient had normal corpuscles. The fact that in my own case two members of the same family have been observed to show this remarkable cellular deformity, I think is very strong evidence in favor of the theory that the condition is a congenital anatomical defect.

St. Luke's Hospital.

THE PITUITARY GLAND IN EPILEPTICS*

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SONYEA, N. Y.

It seems probable that the time is past when we can group as due to a single cause or group of causes the numerous nosological types which in the past we called epilepsy, but which to-day we call the epilepsies, or epileptic syndromes. Our efforts, if they are to be ultimately profitable, must now be directed to the clinical study of the disease and to the construction of an adequate classification. Even in the smaller groups into which we shall divide the epilepsies, we shall find, in each, the result of the interaction of many factors, differing more or less in the individual case; in fact, the epilepsies are to be regarded as due to a summation of causes, rather than as a manifestation of some one single etiological factor.

At present, epilepsies are generally classed as symptomatic and idiopathic (also genuine or essential). In the latter group are placed all cases in which there is no obvious anatomical lesion or extrinsic condition at the bottom of the disease. Considerable time and space have been devoted to theorizing on the etiology of this residual group of epilepsies, and among the most attractive of the suggestions made is that of disturbed metabolism, especially disturbances of the glands of internal secretion.

The necropsy material available at the Craig Colony represents a considerable opportunity for the study of anatomical conditions associated with the disease, and we have for some time been collecting material which might cast some light from an anatomical point of view on the conditions of the ductless glands in epilepsy. The thyroid and pituitary glands were the only ones showing any great change in appearance; both of these showed more or less variation from what might be considered an average or normal type. In this paper we shall deal with the anatomical conditions found in the pituitary gland of epileptics and with certain clinical findings which may be of interest in connection with the rôle played by this gland.

ANATOMICAL FINDINGS

The sella turcica has not as a rule been enlarged; ordinarily, the gland has completely filled it. There has, however, been a distinct group of cases in which there has been a marked difference between the size of the sella and the size of the gland. In these cases the dura

* Submitted for publication, Jan. 20, 1914.

is seen pouched down into the sella, instead of the more usual flat membrane between the clinoid processes. When this pouching is found, the gland may be flattened (scaphoid) in shape, but small glands or large fossae may also account for the condition in different cases. In only one such case have we taken measurements of the sella;

TABLE 1.—Dimensions and Weights of Pituitary Glands

Necropsy No.	Width (Lateral) cm.	Ant.-Post. cm.	Thickness cm.	Weight gm.
390	1.60	1.05	0.55	0.5938
392	1.42	0.966	0.645	0.560
393	1.04	0.775	0.888	.....
395*	1.20	0.7	0.5	0.281
396	1.10	0.9	0.5	0.345
398	1.50	1.4	0.3	0.603
400	1.40	1.0	0.6	0.504
401	1.5	0.9	0.6	0.586
403	1.20	0.8	0.5	0.504
404	1.50	1.1	0.4	0.454
405†	1.65	1.2	0.7	1.032
406	1.40	1.1	0.7	0.61
407	1.3	1.0	0.5	0.428
Average...	1.37	0.98	0.56	0.541
High.....	1.65	1.40	0.88	1.032
Low.....	1.04	0.7	0.3	0.281

* Smallest. † Largest.

TABLE 2.—Additional Gland Measurements

Necropsy No.	Width cm.	Ant.-Post. cm.	Thickness cm.	Weight gm.
416	1.75	1.55	0.47	....
421	1.50	0.85	0.55	0.51
422	1.40	0.80	0.60	0.410
423	1.60	1.05	0.55	0.612
424	1.30	0.90	0.55	.....
425	1.20	1.00	0.60	0.489
426	1.50	1.30	0.50	0.620
427	1.60	1.10	0.65	0.735
428	1.30	1.10	0.60	0.480
Average.....	1.46	1.07	0.56	0.551

they were as follows: between anterior clinoid processes, 28.3 mm.; between posterior clinoid processes, 17.5 mm.; between optic foramina, 19.8 mm.; from optic foramen to posterior clinoid process, 15.5 mm.; width in sagittal plane, 15.5 mm.; depth, 16.6 mm. The gland itself in this case (A 416) measured 17.5 by 15.5 by 4.7 mm. The woman

in whom this was found was decidedly fat; ovaries small and fibrous, uterus unicornus; age at death 44 years. Also, in a case of internal hydrocephalus, a much-pouched dura was found. It is not cases, however, in which increased intracranial tension is apparently present that are interesting, but those in which the pouching is without apparent cause other than a disparity between the bony fossa and the gland.

We regret that we have not a larger series of weights and measurements of pituitaries to report. A small series were measured at the colony by Mr. Worthing of the 1913 medical class of Syracuse University, and a few additional have been recorded (Tables 1 and 2).

Fig. 1.—Case A-356. These figures show large adenomatous area in the pars glandularis, no symptoms noted.

Dock[1] quotes Zander as giving the size of the pituitary gland as variable from 6 to 10.5 mm. in sagittal, from 10 to 14.5 mm. in vertical and from 5 to 9.75 mm. in transverse diameter, and weighing 0.6 gm. Our figures are within this range, though the weight tends to be lower in our series.

Our figures compare somewhat unfavorably with the dimensions and sizes given by Biedl:[2] anteroposterior, 14.4 mm.; lateral, 21.5 mm.; thickness, 5.5 mm.; weight, from 0.59 gm. to 0.731 gm. (as great as

1. Dock: Modern Medicine (Osler) Lea and Febiger, 1909, vi, 463.
2. Biedl: Innere Sekretion, Urban and Schwarzenberg, Berlin, 1910, p. 281.

1.65 gm. in multiparas). The twenty-two glands recorded in this paper appear to be somewhat below the average of these figures.

No large *tumors* of the pituitary have been found at the colony, but in three cases large tumor-like structures have been found. There were no clinical symptoms in any of these cases, and the detailed case notes will therefore not be given; it should be stated that the condition was not suspected, and thus significant clinical conditions may have escaped notice. Figures 1, 2, 3 and 7 show the nature of the process in each case.

Fig. 2.—A-295. Adenomatous area in pars glandularis. No clinical data.

One of the most striking variations in the appearance of sections of the pituitary is variation in the blood-content of the gland. Certainly, in many cases it considerably exceeds the normal. All degrees are present and an uneven distribution of the congestion is not uncommon (Fig. 4).

No particular cell type can be said to predominate in the glands examined in our series. There are occasionally glands in which the cyanophil cells are considerably more common than the average.

The ordinary illustrations and descriptions of the pituitary do not show much connective tissue[3] in the pars anterior. The acini seem normally to be supported by a very slender framework, but in the cases examined at the colony, increases of connective tissue seem to be decidedly common. These are of two types, diffused and localized.

As shown in the photomicrographs (Figs. 5 and 6), there are found extremely irregular spider-like masses of connective tissue in the middle of the pars anterior. These are made up of dense hyaline

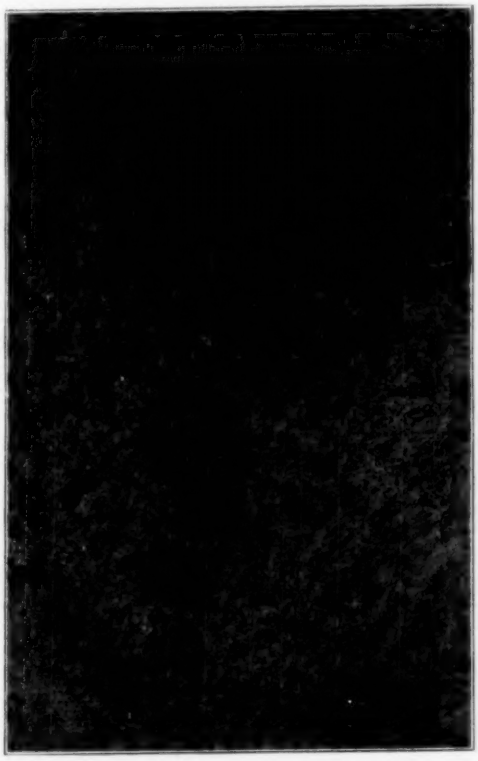

Fig. 3.—Case A-405. Section of "tumor" showing that it is composed of bands of dense connective tissue, markedly fibrous, between which are acini, narrowed and compressed. This patient also had a glioma of the temporo-sphenoidal region.

3. Claude, H., and Schmiergeld, A.: (L'encéphale, Jan. 10, 1909, abstracted in Epilepsia, ii, 207), say that the hypophysis often presents sclerosis, etc. Cushing, in a personal communication, also speaks of the great variety of changes which may be found in the gland.

tissue, with no great amount of fibrillar structure. Within them, in the central portion, are blood-spaces, and from the borders, irregular trabeculae are sent out which gradually break up and disappear between the acini. Near the central mass, these trabeculae often enclose acini, and the latter are apt to show an excess of cyanophil cells. These "spiders" or "islands" tend to be located in the center of each lateral half of the pars anterior; sometimes only one is present. As a rule, these structures seem to have no connection with the capsule

Fig. 4.—Case A-322. Enlarged blood-spaces.

of the gland, but in a few instances there has appeared to be a connection extending toward the hilum of the gland, if we may so designate the hollow in which the pars posterior is placed; in one case, this connection was quite definite and showed indications of canalization by blood-spaces.

The significance of these islands is not clear. They are not invariably found, though this may be due to failure to examine sufficient sections from a particular gland. It seems probable that they are associated with the blood-supply of the pars anterior, and that they

may be residues from the ingrowth of connective tissue during fetal life, described by Frazer.[4]

The diffuse type (Fig. 7) of connective-tissue change is distinctly different and consists of a more or less extended thickening of the interacinar connective tissue. Ordinarily, composed of a few almost invisible fibers, the fibrous tissue between the acini may become almost as thick as the acinus is broad. Not all these appearances, however,

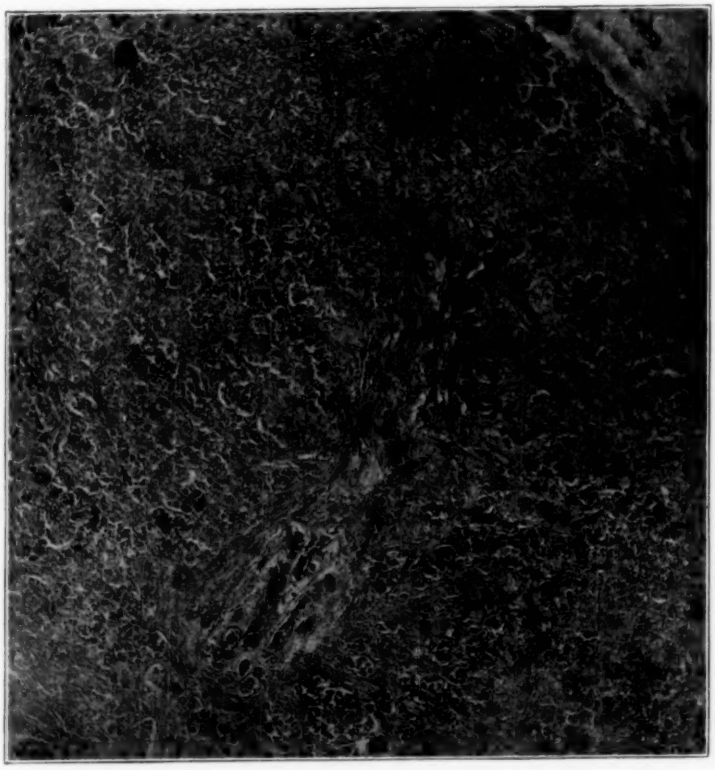

Fig. 5.—Case A-373. "Islands" of connective tissue.

are genuine diffuse change. If the reader will examine Figure 5, and imagine a section made close to the island, he will see that the section would have the appearance of connective-tissue increase between the acini, on account of the trabeculae coming from the island which has been cut across. The island, of course, would not show. Serial sec-

4. Frazer: Lancet, London, Sept. 28, 1912.

tions, or at least a goodly number of sections from each gland, are necessary to the proper examination of this gland.

There is also a distinct tendency toward an increase of connective tissue in the region between the neurogliar and glandular portions. This is shown in Figure 8.

It is of interest that the brothers Wenzel (quoted both by Biedl and by Cushing[5]) looked on colloid collections in the pituitary as the cause of epilepsy. Colloid is almost always present in our glands, but

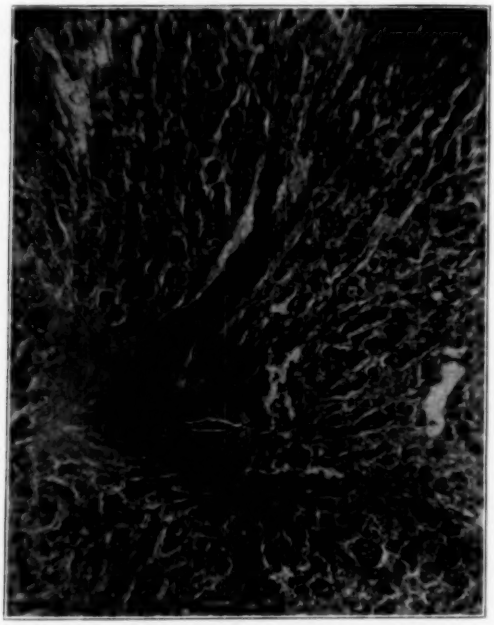

Fig. 6.—Case A.-423. "Islands" of connective tissue.

only occasionally to any extent. These accumulations are usually in the region between the parts of the gland, though occasionally colloid acini are seen in the pars anterior (Figs. 8 and 9).

It will be seen that there are no constant changes in the pituitary gland from an anatomical point of view which have not been elsewhere reported; the connective-tissue "islands" are apparently an exception to this, but their significance is not clear — they are probably connected with the blood-supply. The possibly diminished size of the gland and

5. Cushing, Harvey: The Pituitary Body and Its Disorders, Philadelphia, J. B. Lippincott Co., 1912.

an occasional large sella turcica appear the most striking signs of pituitary change; the tumor-like structures are of unknown significance in the absence of clinical symptoms.

CLINICAL DATA: BLOOD-PRESSURE AND SUGAR TOLERANCE

Cushing[5] advances the hypothesis that certain cases of epilepsy are associated with insufficiency of the pituitary gland. While it is not new to have the glands of internal secretion indicated as of importance

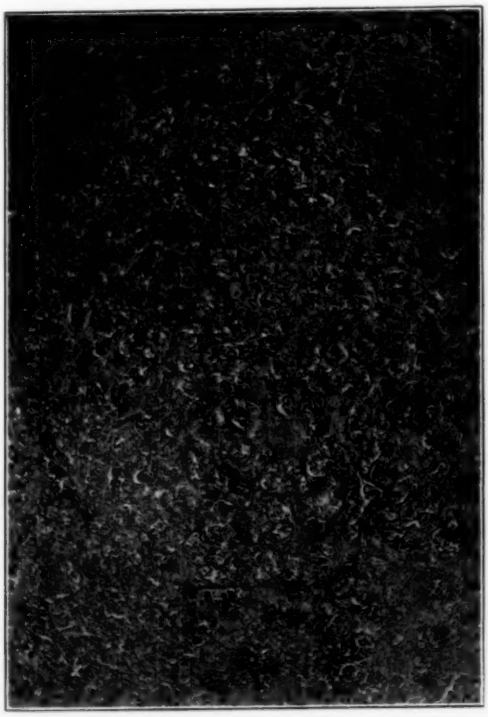

Fig. 7.—Case A-373. Diffuse interacinar connective tissue.

in the production of epilepsy, the designation of a particular one and the definite characterization of its rôle as one of insufficient activity, rather than of perverted activity, and the presentation of a quite definite clinical picture of the condition, make Cushing's hypothesis worthy of careful consideration.

He sums up the basis for his hypothesis as follows:

1. Horsley found that the cortex of hypophysectomized dogs was more sensitive to stimulation than that of normal animals.

2. In a number of Cushing's hypophysectomized animals, a tendency to convulsions was observed.

3. Epilepsy is a frequent sequel of cranial injuries, and in certain of these, the pituitary is damaged.

4. Epilepsy is a frequent accompaniment of hypopituitarism.

5. The secretion of the posterior lobe apparently enters the cerebrospinal fluid and thus reaches the brain. Thus a scar or tumor, etc., may prevent the contact of the secretion of the posterior lobe with the nerve-cells, with resulting alteration in their stability.

Fig. 8.—Case A-423. Amount of connective tissue sometimes seen between the two portions of the gland. Some of the rounded spaces contain colloid.

6. Many epileptics present symptoms of hypopituitarism, and administration of the gland substance modifies the seizures.

Cushing apparently offers four cardinal symptoms of states of pituitary hypoactivity: (1) high sugar tolerance; (2) subnormal temperature, slowed pulse and low blood-pressure; (3) drowsiness, and (4) asthenia.

Of the characters indicated by Cushing, subnormal temperature has been very frequently observed in epileptics, especially when combined

with low mental grade and the accompanying asthenia. Reuben quotes from the literature that hypophysectomized dogs may have a temperature of 20 C. (68 F.) just before death. We believe that it may be accepted that subnormal temperatures are not uncommon among epileptics.

The literature contains a few references to blood-pressure in epileptics. Spratling[6] reports for thirty-three cases between 10 and 43 years of age, readings of from 115 to 135 mm. of mercury. Turner,[7]

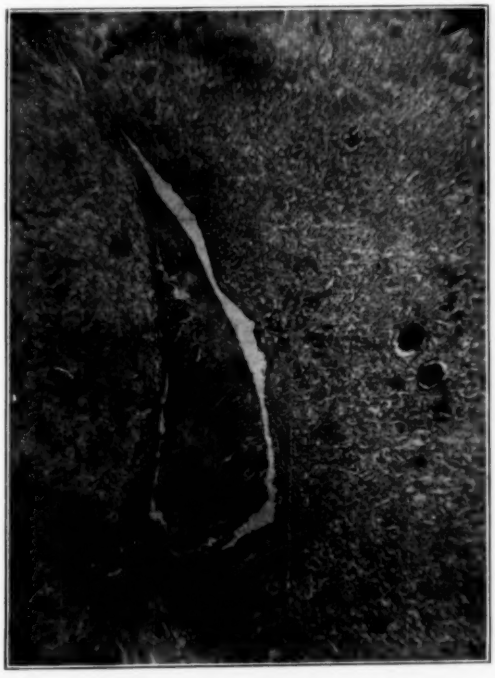

Fig. 9.—Case A-336. Colloid accumulation in a cleft between the two parts of the gland.

taking from 110 to 130 mm. as the normal average, reports that he found one epileptic with high and four each with normal or low blood-pressures in nine cases. Besta[8] reported 63 per cent. of his cases as having higher than normal blood-pressure. No data are given as to

6. Spratling, W. P.: Epilepsy and Its Treatment, Philadelphia, W. B. Saunders & Co., 1904, p. 172.
7. Turner: Jour. Ment. Sc., 1907, liii, 793.
8. Besta: Jour. Ment. Sc., 1907, liii, 404.

the number of cases examined or his normal standard. Pollock and Treadway[9] report forty-one cases, of which eighteen had a systolic pressure of 120 or below and twenty-three ranged from 125 up to 200. From these rather meager reports it would seem that there was no striking change in the blood-pressure of epileptics as a class.

Our own series bears this out. Our results, using a group of sixty-six epileptic imbeciles, are given in Table 3. Two cases in the 12-to-20 year group, and one in the 31-to-40 group, were excluded from the averages on account of the excessively high figures which they showed.

TABLE 3.—PRESSURE BY AGES

Year Group	Systolic	Diastolic	Pulse-Pressure	Cases
To 20 inc.	115	76	37	15
30	126	82	41	27
40	127	78	43	13
50	132	92	40	7
59	197	107	87	1

Grouped by the systolic pressure, the cases arrange themselves as follows:

Below 100 mm., 1		To 140 mm., 13	(19.60 per cent.)
To 110 mm., 4		To 150 mm., 6	
To 120 mm., 17	(25.75 per cent.)	To 187 mm., 1	
To 130 mm., 23	(34.85 per cent.)	To 197 mm., 1	

It is thus seen that low blood-pressures are rather uncommon and that in general the pressures observed agree with the physiological normals.

The diastolic pressures ranged as follows:

From 21 to 30 mm., 7	51 to 60, 9
From 31 to 40 mm., 24	61 and up, 2
From 41 to 50 mm., 23	

In a few cases we have observed the effect on blood-pressure of doses of pituitary whole gland extract by mouth. The changes are not at all characteristic and are influenced by the difference in the time of year — the control observations having been made during cold weather and these while under treatment in warm weather. Reversing the expectation based on the known pressor influence of pituitary extracts, the more striking change is a slight lowering of the blood-pressure or no change of blood-pressure. This portion of the work we do not regard as at all accurate, on account of the seasonal changes and the short periods of administration of the gland.

9. Pollock, L. J., and Treadway, W. L., A Study of Respiration and Circulation in Epilepsy, THE ARCHIVES INT. MED., 1913, xi, 445.

The question of sugar tolerance in epileptics is one of more difficulty. The literature contains comparatively little of assistance as to either the normal or the pathological side.

The normal assimilation limit is variously stated, but appears for dextrose to be from about 100 to 300 gm., or a possible average of 2.5 gm. dextrose for each kilogram of body-weight. There are, however, factors which influence the assimilation limit and which are hard to control and estimate:

THE RATE OF INTRODUCTION AND ABSORPTION OF THE SUGAR

The kind of sugar influences this as well as the physical characters of the solution in which the sugar is administered. For absolutely accurate results it would be desirable that the dose and volume of the solution should always be uniform. This is, of course, obviously impossible, since the body-weight varies among individuals. It must be remembered that volume and concentration of the solution introduce variable factors. The amount of glycogen stored in the body also influences the utilization of sugar, together with the amount of muscular work being done during the experiment. The effects of hunger — hunger glycosuria — we may leave out of consideration. It is said that the external temperature influences the utilization of sugars, a high temperature favoring an alimentary glycosuria. Individual peculiarities also probably play an important rôle.

Raimann reports a raised assimilation limit in idiocy, mania, paranoia, in epileptics and in alcoholics after the disappearance of the mental disturbance. Strauss reports no especial tendency to alimentary glycosuria in hysteria and epilepsy. Sigmund[10] noted a transitory glycosuria in 7.4 per cent. of epileptics.

It may be noted that in the course of several thousand examinations of the urine of epileptics, glycosuria has been an extremely rare finding at the Craig Colony.

In the work reported in the present paper, test doses were administered in the form of a sirup, flavored with lemon extract to appeal to the palate. The gross weight of dextrose used was disregarded as we found that the commercial dextrose used did not titrate at its expected strength; therefore each individual batch of sirup was carefully titrated against carefully standardized Fehling's solution. Sirups ranged in strength from about 45 gm. to 70 gm. to 100 c.c.

In our work the dose was administered about 10 or 11 a. m.; these patients have breakfast between 6:30 and 7 o'clock, so that the stomach should have been fairly empty at this time. We found that many patients vomited at dinner-time, and when giving larger doses, it was decidedly a wise procedure to refuse dinner to the experimental per-

10. Sigmund: Handbuch der Biochemie, iv, part ii, 153.

sons. At first urines were collected at frequent intervals, but we found that all practical purposes were served by samples taken at 2 and 4 p. m., respectively. Control urines taken before the doses were given in no case showed glycosuria.

In examining the urine samples, Fehling's test was used entirely. Dextrose is apparently present in normal urine to a very small amount, but is not recognizable by Fehling's solution, so that it does not enter into our work. Simon states that the ordinary tests, including Fehling's, are worthless for detecting the occurrence of alimentary glycosuria, and directs the use of the fermentation test as the determining test. He assigns no reason for this. If, however, we consider the utilization of dextrose and the qualities of the tests employed, we shall have a much better idea of the value of the several testing methods.

Dextrose is completely utilized and is excreted as water and carbon dioxid. This change does not immediately take place, however, some dextrose being deposited as glycogen and some being only partially oxidized, forming glycuronic acid. The latter product may appear in the urine if it is formed in excessive quantities, and it is also a fair assumption that if the amount of dextrose offered for assimilation is excessive, more of the glycuronic acid will be formed and excreted. The free acid is not fermentable by yeast, but readily reduces Fehling's solution without boiling. Glycuronic acid does not appear free in the urine, but in combination with phenol, indoxyl, or skatoxyl, and in this form it is only very slowly reducing for Fehling's solution and then only at boiling temperatures. Dextrose is easily reduced by Fehling's solution without boiling and is fermentable by yeast. The use of the fermentation test would exclude glycuronic acid, but the same may be done by performing Fehling's test properly, that is, without boiling. The latter test has the advantage, however, that by the later thorough boiling of it, the presence of glycuronic acid may be recognized. There are other bodies which may give small reductions in this part of the test; when overdoses of dextrose are being given, we may regard these as negligible.

In our work we have used the Fehling test, both with and without boiling, in the belief that the dextrose or an excess of glycuronic acid were equally significant. Cases in which the tests were marked positive with a question-mark indicate reductions which have occurred after boiling. These reactions were characterized by the production of yellow or orange precipitates, and never has a dirty-green cloudiness, which so often occurs, been accepted as a reduction, even though reduction may occur in such a test if allowed to stand a sufficient length of time.

The proportion of positive results among the higher ratios is evident (Table 4), but even so, the number whose tolerance was passed is very much smaller than the number of those who gave negative results.

Of the two positives indicated as occurring at ratios between 2 and 3 gm. per kilogram, it must be remarked that in one, there was apparently a transitory renal disturbance, as indicated by an excess of cylindroids, casts and leukocytes. This patient afterward tolerated a much larger dose, at a time when the urine was clear. In the other instance, the test was very doubtfully positive, and is the only test on that patient.

Theoretically, and judging from the results of Cushing's work, administration of gland extract should cause a lowering of the assimilation limit, and doses of sugar given during administration of gland substance should produce glycosuria at a much lower rate of "grams per kilogram" than without the drug. In our experiments on this end

TABLE 4.—SIZE OF DOSES OF DEXTROSE, IN TERMS OF GRAMS PER KILOGRAM OF BODY-WEIGHT, AND RESULT

Grams Per Kg.	Total Cases	Positive Result
2 to 3	13	2
3 to 4	26	0
4 to 5	13	1
5 to 6	14	5
6 to 7	10	2
7 to 8.15.....	8	2
	84	12

of the subject, we have considered doses of 2.5 gm. per kilogram as representing the normal limit. The amount of gland substance required to produce glycosuria with this dose should represent the deficiency of the patient's own gland. Table 5 gives the results of our work in this direction. It will be noted that in the last three groups, the amount of dextrose used is considerably increased. This was done as we found that the lower ratios were not giving results, and rather than increase the dose of the expensive gland preparation we preferred first to increase the sugar and try and obtain positives in this way.

It will be seen that the tolerance is not lowered in the majority of these cases. The ratio of positives is not much different from that seen in the control series for maximum tolerance, namely, one-seventh of the cases in each group show positive; but a comparison of the amounts of sugar used will show that the positives obtained with coincident gland administration were, on the whole, obtained with much

lower amounts of sugar. Probably the small doses of gland substance are too small, and we see that the positives in the groups taking from 20 to 30 grains three times a day, seventeen in all, show four positives, or nearly one-quarter. These cases were given sugar between ratios of 3.08 and 4.95. Comparing with the previous table, we see that between 3 and 5 there were thirty-nine cases with only one positive among them.

TABLE 5.—Results of Gland Administration

Grains T.I.D.	Experiments	Ratio Used	Result
3	9	2.35 : 2.85	0
6	7	2.69 : 3.09	1 positive
10	37	2.53 : 4.8; One case, 1.62	5 positive
15	1	3.7	0
20	12	3.08 : 3.48	3 positive
30	5	4.0 : 4.95	1 positive
	71		10 positive

Some of the particular cases may be cited from the table:

Babcock, positive (?) at 7.06 per kilogram; positive with 10 grains of gland, ratio, 2.76 negative with 30 grains of gland, ratio, 4.48.

Neville, positive 2.3 grams — urine shows casts, etc.; negative at 2.2, 2.7, 3.9; positive with 6 grains t. i. d., and 2.82 gm.; negative with 10 grains t. i. d., and 3.68 gm.

Wilde, negative with 5.9 gm. sugar per kilogram; with 20 grains gland t. i. d., gave doubtful negative with 3.39 gm. sugar.

Klotz, negative with 6 gm.; positive with 10 grains t. i. d., and 3.1 gm. sugar; negative with 10 grains t. i. d., and 3.1 gm. sugar; negative with 30 grains t. i. d., and 3.7 gm. sugar.

McDermott, negative with 8.15 gm. sugar; positive with 10 grains gland t. i. d., and 2.72 gm. sugar; negative with 30 grains gland t. i. d., and 4.75 gm. sugar.

McArthur gave negative with 10 grains gland t. i. d., and 2.76 and 4.13 gm. sugar; positive with 10 grains gland t. i. d., and 2.66 gm. sugar.

It will be seen from these instances that the reaction to this set of experiments has not been uniform in all cases. It is evident that some variable factor either in the method or in the patient is causing an apparent variation of the assimilation limit for dextrose. It will require considerably more work with these patients to determine the basis of these variations.

It seems reasonable, however, to conclude, even from the work at this stage, that there is a definite and marked elevation of the assimilation limit in these patients. Whether or not this has any relation to the activity of the pituitary gland is not shown clearly enough at present to permit any statement.

THE SPECIFIC ROLE OF FOODS IN RELATION TO THE COMPOSITION OF THE URINE*

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INTRODUCTION

The influence of individual foods on the composition of the urine has been studied from several points of view. Many of the relations have been satisfactorily determined.

It is a matter of common knowledge that the urine of herbivorous animals is alkaline to litmus, while that of the carnivora is acid in reaction. Human urine, likewise, is normally acid. The alkaline urine of herbivora has been supposed to result from the vegetable foods on which they live. Similarly, the acid reaction of the carnivorous urine was referred to the meat diet of these animals. What is present in these foods that may be held responsible for the differences in urinary acidity? The excess of base-forming elements in vegetables and of acid-forming elements in meats at once suggests an answer. It was not until Sherman and Gettler[1] made more complete ash analyses of a large number of foods that the importance of this point was sufficiently impressed. Their studies showed that the vegetables and fruits, on burning, leave an ash preponderating in the basic elements, sodium, potassium, calcium and magnesium. The cereals, meat and fish foods give an acid-reacting ash because of a predominance of the acid-forming elements. The important fact must not be overlooked that the ash of plant foods may be either basic or acidic. Throughout this investigation, the analyses just referred to have been kept in mind (Table 1).

Another factor which may directly affect the acid formation within the body is the protein intake. Its content of sulphur and phosphorus leads to the production of acids, which require that a certain amount of base be supplied for neutralization. On the other hand, Robertson[2] has shown that the serum proteins are efficient in neutralizing acids. He found these body proteins to be about one-fifth as capable of neutralizing acids as are the phosphates and bicarbonates.

* Submitted for publication, May 2, 1914.
* From the Sheffield Laboratory of Physiological Chemistry, Yale University.
* Reported before the American Society of Biological Chemists, Philadelphia, Dec. 31, 1913.

1. Sherman and Gettler: Jour. Biol. Chem., 1912, xi, 323.
2. Robertson: Jour. Biol. Chem., 1910, vii, 351.

TABLE 1.—Ash Analyses of Sherman and Gettler: Excess of Acid-Forming or Base-Forming Elements[1]

Articles of Food	Excess Acid or Base in Terms of Normal Solutions			
	Per 100 Gm.		Per 100 Calories	
	Acid c.c.	Base c.c.	Acid c.c.	Base c.c.
Almonds	.....	12.38	.....	1.86
Apples	.....	3.76	.....	5.98
Asparagus	.....	0.81	.....	3.65
Bananas	.....	5.56	.....	5.62
Beans, dried	.....	23.87	.....	6.92
Beans, lima, dried	.....	41.65	.....	12.08
Beets	.....	10.86	.....	23.57
Cabbage	.....	4.34	.....	13.76
Carrots	.....	10.82	.....	23.91
Cauliflower	.....	5.33	.....	17.48
Celery	.....	7.78	.....	42.17
Cherry juice	.....	4.40		
Chestnuts	.....	7.42	.....	3.19
Corn, sweet, dried	5.95	.....	1.77	
Crackers	7.81	.....	1.95	
Currants, dried	.....	5.97	.....	1.85
Eel	9.89	.....		
Eggs	11.10	.....	7.55	
Egg white	5.24	.....	9.52	
Egg yolk	26.69	.....	7.08	
Fish, haddock	16.07	.....		
Fish, pike	11.81	.....		
Lemons	.....	5.45	.....	12.32
Lettuce	.....	7.37	.....	38.69
Meat, beef, lean	13.91	.....	12.10	
Meat, chicken	17.01	.....		
Meat, frog	10.36	.....		
Meat, pork, lean	11.87	.....		
Meat, rabbit	14.80	.....		
Meat, veal	13.52	.....		
Meat, venison	15.83	.....		
Milk, cow's	.....	2.37	.....	3.44
Muskmelon	.....	7.47	.....	18.82
Oatmeal	12.93	.....	3.23	
Oranges	.....	5.61	.....	10.94
Peaches	.....	5.04	.....	12.20
Peanuts	3.9	.....	0.70	
Peas, dried	.....	7.07	.....	1.98
Potatoes	.....	7.19	.....	8.63
Prunes	.....	24.40	.....	8.05
Radishes	.....	2.87	.....	9.79
Raisins	.....	23.68	.....	6.87
Raspberry juice	.....	4.91		
Rice	8.1	.....	3.35	
Turnips	.....	2.68	.....	6.86
Wheat, entire	9.66	.....	3.25	
Wheat, flour	11.61	.....	2.70	

Urinary acidity is dependent on the composition of the blood. This fluid maintains a very constant, slightly alkaline reaction, as has been observed by many investigators. How is its uniform reaction maintained? The most important factor in bringing this about is the presence of salts of carbonic and phosphoric acids. Systems consisting of H_2CO_3, $NaHCO_3$, NaH_2PO_4 and Na_2HPO_4, such as are found in the blood, have great powers for maintaining neutrality (Henderson).[3] Thus, in a phosphate solution, relatively large amounts of base may be neutralized, with very small changes in reaction. The acids of the blood leave the body by two channels, the carbonic going chiefly by way of the lungs. The remaining acids are excreted by the kidneys. The latter organs, therefore, have a very important rôle in relation to the body acids and consequently in the preservation of body neutrality. The case of phosphoric acid serves to emphasize the importance of the kidney's function along these lines. This acid exists in the blood largely as Na_2HPO_4, while it is found in the urine chiefly as NaH_2PO_4. Thus, in passing through the kidneys, a great share of the base has been retained and is again ready for further combination with acid. Since phosphoric acid is one of the chief acids of the urine, the value of this phenomenon is very significant. Of the acids produced in metabolism, only sulphuric removes all of the base required for neutralization. It becomes apparent that the introduction of bases into the body offers a ready supply for the neutralization of acids formed in metabolism. Depending on the quantities introduced, this may significantly change the composition of the blood and, as a consequence, the make-up of the urine. The study of urinary acidity, therefore, becomes highly important.

The true acidity of the urine is due to an excess of H^+ ions in the excretion. In terms of physical chemistry, an excess of H^+ ions in solution causes acidity, while a surplus of $\overline{OH}$ ions produces alkalinity. Whenever there is an equal number of H^+ and $\overline{OH}$ ions present, the solution becomes neutral.

H^+ ion concentration is expressed as gram of ionized H per thousand grams of water. A neutral solution has a H^+ of 1 times 10^{-7} or 0.000,000,1 gm. per liter. As a matter of convenience in recording, the H^+ is often expressed by using the logarithmic notation of Sörensen. Thus, at neutrality the H^+ is 7.00. As the H^+ increases, this value decreases, and with an increasing $\overline{OH}$ the value increases. In our protocols, the H^+ is expressed in this fashion.

Not until Henderson and Palmer[4] developed their indicator method for determining the H^+ of the urine, have we possessed a ready and

3. Henderson: Am. Jour. Physiol., 1908, xxi, 427.
4. Henderson and Palmer: Jour. Biol. Chem., 1913, xiii, 393.

accurate method for the estimation of true urinary acidity. Formerly, the H^+ was found by the laborious gas-chain method. Because of the complications involved, this procedure was not suitable for general use. The indicator method makes use of the well-known fact that the color of an indicator varies with changes in H^+.

Thirteen solutions of known H^+ are prepared, the concentration of the most acid being 4.70 and that of the most alkaline 9.27. Corresponding volumes of the standards and of the urines under investigation are diluted to a definite volume, and the same amount of indicator added to each. The color of the urine sample is then matched with the standards and its position in the series located. Since equal volumes of the standards and of the urines are used, any two having the same color and intensity must have the same H^+. The method is rapid and is especially applicable to experiments in which the subjects are maintained on a uniform diet, for one is then able to forecast in what range of H^+ the urines will fall. The necessity of trying different ranges and indicators is therefore eliminated.

Using this method, Henderson and Palmer[4] reported that the H^+ of urines of normal individuals living on a mixed (?) diet ranges from 4.82 to 7.45, with an average of 6.03. Very recently (1914), these authors[5] have published further observations on 122 specimens, the average H^+ of which was 5.94. The mean value of those previously recorded and of that found in their latest studies is 5.98. These authors believe that under general conditions of activity and diet the H^+ is equal to 6 ± 0.1. They also stated that under pathological conditions the tendency is for the H^+ to become greater. This was especially observed in cardiorenal cases, in which the average value of 5.33 was obtained.

At this point, it may be desirable to consider the relation of H^+ to the urinary acidity as determined by the titration methods which are commonly used. Titration, with a base, does not measure the true acidity. It merely gives the excess of acid substances, as shown by some indicator. That titration methods are not without objection is easily gleaned from the admirable discussion by Henderson:[6]

> Without exception such procedures consist in titrating to the reaction which chances to be a convenient "end-point" of a particular indicator. But such a point is in itself quite without necessary physiological significance, for there is in the nature of things no relation between any physiological constant or process and the reaction at which phenolphthalein, or litmus, or alizarine, or any other indicator changes color sharply. Each of these concentrations of ionized hydrogen is dependent in an indeterminate way on the chemical constitution of the indicator, and upon nothing else. Any other relationship is

5. Henderson and Palmer: Jour. Biol. Chem., 1914, xvii, 305.
6. Henderson: Jour. Biol. Chem., 1911, ix, 403.

purely accidental. Nor is there even in chemical theory that prescription of a particular indicator which may always be found in the case of the titration of any simple solution. This fact is amply attested by the difficulties which have been encountered in devising a suitable titration method to estimate the excess of acid over base in urine. Among the urinary constituents are some whose "neutralization" is incomplete at any possible end-point. In solutions which are just pink with phenolphthalein ammonia is free in measureable amount, and the proteins and amino-acids are combined with a considerable and uncertain quantity of base. Between such alkalinity and the acidity of the methyl orange end-point the phosphates and many other substances are combined with varying amounts of base. Finally at a more acid reaction hippuric acid, lactic acid, and other substances are present partly as salts and partly free, while, on the other hand, the proteins and their derivatives are in part united with acid.

Phenolphthalein is the indicator most generally used, because it marks most nearly the end of a number of chemical reactions.

To show that H^+ and titratable acidity are very different, one needs only to consider solutions of the common acids. Normal solutions of hydrochloric and acetic acids will require the same amount of base for neutralization, but the H^+ of the hydrochloric is much greater than that of the acetic. This is due to the fact that the molecules of hydrochloric are dissociated to a greater extent. Acids which have a small ionization constant are termed weak acids. The urine resembles the weak acids, such as acetic, but its H^+ is less and its capacity for combining with bases greater. This is due to the presence of weak acids and their salts, especially NaH_2PO_4 and Na_2HPO_4.

Organic salts of the alkalies are widely employed as therapeutic agents, those most commonly used being the bicarbonate and citrate of sodium. Many of the organic acids are oxidized to carbonates in the body. The carbonic acid is given off through the lungs, the base remaining to combine with acids produced by the body. It has long been known that the urine can be rendered alkaline to litmus by the administration of alkalies. The extent of this reduction in H^+ has been determined by Henderson and Palmer.[7] On giving alkalies, such as the citrate and bicarbonate of sodium, they were able to obtain a H^+ of 8.70, which corresponds to the alkalinity of a solution of 0.01 N Na_2HPO_4. Hanzlik and Collins[8] observed a similar effect during their studies on the conversion of hexamethylenetetramin into formaldehyd in the urine.

The belief that ammonia is produced within the body to neutralize the acid products of metabolism is generally accepted. Supporting this conclusion is the often-observed fact that the output of ammonia in the urine is decreased when alkalies are given. That is, the alkalies

7. Henderson and Palmer: Jour. Biol. Chem., 1913, xiv, 81.

8. Hanzlik, P. J., and Collins, R. J.: Hexamethylenamin: The Liberation of Formaldehyd and the Antiseptic Efficiency under Different Chemical and Biological Conditions, THE ARCHIVES INT. MED., 1913, xii, 578.

TABLE 2.—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H·]	Ammonia N, gm.
SUBJECT B					
April		1.013	216	7.48	0.234
14	1,500	1.017	288	7.14	0.323
15	1,075	1.012	267	7.38	0.314
16	1,450	1.020	271	6.90	0.309
17	890	1.015	266	7.14	0.316
18	1,145	1.016	284	7.38	0.292
19	1,060				
SUBJECT W					
April					
14	890	1.022	253	7.43	0.224
15	1,070	1.021	300	7.14	0.283
16	955	1.022	264	7.38	0.287
17	820	1.024	253	7.14	0.236
18	930	1.022	286	7.38	0.268
19	880	1.024	264	7.38	0.286

TABLE 3.—Basal—

SUBJECT B					
April					
7	1,150	1.020	221	7.48	0.234
8	1,020	1.023	196	7.74	0.221
9	1,135	1.020	200	7.74	0.231
10	1,260	1.019	202	7.74	0.212
11	1,250	1.018	190	7.74	0.270
12	1,350	1.016	216	7.74	0.243
13	1,150	1.019	212	7.74	0.248
SUBJECT W					
April					
7	925	1.026	204	7.48	0.289
8	775	1.027	210	7.43	0.279
9	1,100	1.024	180	7.74	0.211
10	1,315	1.020	195	7.74	0.221
11	1,220	1.019	190	7.74	0.264
12	1,345	1.019	194	7.74	0.242
13	1,285	1.021	206	7.74	0.201

TABLE 4.—

SUBJECT B					
May					
26	1,210	1.015	305	6.70	0.334
27	1,330	1.013	229	6.80	0.279
28	1,300	1.014	208	7.14	0.218
29	1,360	1.015	250	7.48	0.245
30	1,040	1.018	225	7.48	0.237
SUBJECT W					
May					
26	835	1.024	294	6.70	0.310
27	975	1.021	230	6.80	0.293
28	920	1.023	265	7.38	0.298
29	980	1.023	261	7.48	0.226
30	860	1.025	248	7.48	0.206

—Basal Diet

Total N. gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
9.40	0.422	0.781	+0.359	Basal diet. Graham crackers, 100 gm. Dairy-butter, 25 gm. Whole milk, 400 c.c. per meal. For supper one soft-boiled egg and one raw apple extra.
10.25	0.459	0.432	—0.027	
10.53	0.438	0.718	+0.280	
10.27	0.490	0.443	—0.047	
10.59	0.440	0.539	+0.099	
10.35	0.447	0.435	+0.012	
8.87	0.377	0.604	+0.227	Basal diet. Graham crackers, 100 gm. Dairy-butter, 25 gm. Peanut-butter, 10 gm. Whole milk, 400 c.c. each meal. For supper one soft-boiled egg and one raw apple extra.
11.06	0.430	0.585	+0.155	
10.89	0.466	0.669	+0.203	
11.02	0.433	0.478	+0.045	
12.00	0.425	0.492	+0.067	
11.40	0.438	0.588	+0.150	

—Diet with Potatoes

10.42	0.503	1.13	+0.627	Basal diet with 750 gm. baked potatoes a day.
10.04	0.494	1.09	+0.596	
10.20	0.508	1.27	+0.762	
10.81	0.480	1.39	+0.710	
11.18	0.485	1.44	+0.955	
10.64	0.499	1.54	+1.04	
10.29	0.492	1.03	+0.538	
11.60	0.459	0.885	+0.426	Basal diet and 600 gm. baked potatoes a day.
9.81	0.406	0.564	+0.158	
11.15	0.472	1.230	+0.758	
10.82	0.440	1.670	+1.230	
10.41	0.444	1.360	+0.916	
11.12	0.520	1.730	+1.210	
10.10	0.469	1.580	+1.110	

—Potato Ash

10.47	0.479	0.418	—0.061	Potato ash corresponding to 750 gm. of baked potatoes begun, May 28.
9.27	0.412	0.614	+0.202	
9.20	0.453	0.973	+0.520	
10.08	0.472	1.080	+0.608	
9.22	0.408	0.745	+0.337	
11.10	0.476	0.448	—0.028	Potato ash corresponding to 600 gm. of baked potatoes, beginning on the third day.
10.20	0.450	0.654	+0.204	
10.07	0.493	0.533	+0.040	
11.21	0.434	0.720	+0.286	
9.71	0.372	0.690	+0.318	

supply a not insignificant amount of the bases required for neutralization, and the ammonia formation is consequently reduced. Janney[9] has reported cases in which doses of 15 gm. $NaHCO_3$ produced a decrease in the output of ammonia to one-third of its normal value. Using larger amounts, he was able to practically suppress the ammonia excretion.

These effects on H^+ and ammonia excretion, which are referable to the intake of bases, are very striking. They give an idea as to the cause of the varying reaction of the urine. In general, foods are burned by the body much as in the crucible, an inorganic residue being the product in both instances. The ash is alkaline in the case of vegetables and fruits and acid when meats and cereals are consumed. Theoretically, we are led to expect that the eating of potatoes, which yield a strongly alkaline ash, will have the same effect on H^+ and ammonia excretion as does the ingestion of comparable amounts of sodium bicarbonate or other suitable bases. Likewise, one would assume that meat-eating should cause the production of a more acid urine. An indication that such may be the case is found in the metabolism experiment conducted by Sherman and Gettler.[1] They reported that the eating of potatoes decreased, while the ingestion of rice, which yields an acid-reacting ash, increased the output of ammonia.

It is common knowledge that experiments conducted *in vivo* and *in vitro* very often differ in their results. In view of the practical importance of this problem, we have made an extended study of the influence of food intake on the acidity of the urine and of the related phenomena.

The tendency for the formation of uric acid sediments in certain urines is often observed. Other urines do not exhibit this phenomenon. Those specimens which produce sediments are always acid in reaction and generally of small volume. Hindhede[10] has reported in numerous papers that urines obtained after eating vegetables of different kinds not only show no tendency to the formation of sediments but have a heightened ability to dissolve uric acid. Potato urines are especially striking in this respect. Other vegetables and fruits which Hindhede has shown to have this same effect on the urine are bananas, carrots, melons, strawberries, tomatoes and rhubarb. Milk urines also exhibit the same phenomenon. On the other hand, urines from a bread or a meat diet not only fail to dissolve more uric acid but deposit some of that already in solution, showing

9. Janney: Ztschr. f. physiol. Chem., 1912, lxxvi, 99.
10. Hindhede: Skandin. Arch. f. Physiol., 1912, xxvi, 384; ibid., 1912, xxvi, 87; Ztschr. f. diätet. u. physik. Therap., 1913, xvii, 592.

that they are supersaturated. Hindhede followed the titratable acidity in these cases and found that there was apparently a relationship between this and the capacity for dissolving uric acid. Those specimens having a low titratable acidity were able to bring added uric acid into solution, while those of high acidity suffered precipitation. This investigator believed that the volume of the urine also had some connection with this phenomenon but was inclined to place more emphasis on the other factor. It seemed that work along this line should be confirmed and extended. Consequently, the solvent power of urine for uric acid has been made a part of our study.

METHODS

H^+ ION CONCENTRATION

The new indicator method of Henderson and Palmer,[4] described above, was used in the determination of true acidity.

SOLUBILITY OF URIC ACID

The procedure used in the estimation of the solubility of uric acid in urine is as follows:

About 125 c.c. of urine are placed in a glass-stoppered bottle. To this is added about 0.5 gm. of pure uric acid. The bottles are then closed and sealed by dipping the necks in melted paraffin. They are placed on a rotating machine and revolved for two hours at room temperature, care being taken not to rotate so rapidly as to produce foam. The urines are filtered and 200 c.c. of the filtrate used for the determination of uric acid. From this result the value for the twenty-four-hour specimen is calculated. This is the total amount of uric acid that the urine is capable of dissolving. We have called this the "total solvent power." The difference between this and the uric acid excreted represents the capacity of the urine for dissolving uric acid, beyond the amount already present. This is recorded as "residual solvent power." A positive sign indicates solution and a negative sign shows precipitation. All determinations of uric acid were made by the Folin-Shaffer method.

This procedure is not open to certain objections which may be offered to Hindhede's[11] method for the determination of the extent of solution. His procedure is outlined below:

Two hundred c.c. of urine are boiled for a few minutes, filtered and again made up to volume with water. Fifty c.c. are transferred to a dried and weighed flask, which contains 100 mg. of uric acid. The flask is placed in a thermostat at 37 C. (98.6 F.) for an hour, and shaken several times during the interval. The contents are filtered,

11. Hindhede: Skandin. Arch. f. Physiol., 1912, xxvi, 384.

TABLE 5.—Alkali, Rice, Wheat—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H·]	Ammonia N, gm.
SUBJECT B					
April					
20	1,210	1.015	198	7.48	0.174
21	1,320	1.015	132	8.00	0.127
22	1,350	1.017	130	8.35	0.113
23	1,155	1.015	166	7.48	0.166
24	1,085	1.018	203	7.38	0.176
26	1,025	1.020	267	6.80	0.197
27	1,045	1.018	297	6.90	0.251
28	1,165	1.021	350	6.80	0.280
29	1,175	1.021	413	6.70	0.395
30	1,150	1.022	378	6.70	0.373
1	1,540	1.018	482	6.50	0.610
SUBJECT W					
April					
20	940	1.024	203	7.48	0.237
21	870	1.025	129	8.00	0.122
22	975	1.028	109	8.35	0.047
23	900	1.025	205	7.38	0.206
24	925	1.023	266	7.14	0.278
26	1,195	1.020	272	6.80	0.244
27	860	1.024	295	6.90	0.299

TABLE 6.—Oranges—

SUBJECT B					
May					
10	1,550	1.014	235	7.48	0.391
11	1,460	1.015	292	7.48	0.333
12	1,200	1.016	293	7.14	0.288
13	1,290	1.015	289	7.38	0.279
14	1,090	1.018	306	7.38	0.275
15	1,130	1.020	249	7.43	0.190
16	1,080	1.020	259	7.38	0.233
17	1,410	1.015	226	7.48	0.246
18	1,150	1.019	290	7.48	0.249
SUBJECT W					
May					
10	1,030	1.024	206	7.43	0.309
11	900	1.026	230	7.43	0.292
12	900	1.025	238	7.38	0.167
13	980	1.023	235	7.43	0.235
14	905	1.026	235	7.48	0.168
15	850	1.028	248	7.43	0.168
16	800	1.028	253	7.43	0.134
17	1,010	1.026	222	7.48	0.206
18	780	1.027	253	7.43	0.178

—Bread, and a Mixed Diet

Total N, gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
9.65	0.413	1.17	+0.757	5 gm. $NaHCO_3$
10.07	0.398	1.50	+1.102	10 gm. $NaHCO_3$
9.93	0.429	2.62	+2.191	15 gm. $NaHCO_3$
9.44	0.422	1.32	+0.898	Rice, 210 gm.
9.19	0.427	0.790	+0.363	Rice, 210 gm.
9.97	0.463	0.523	+0.060	Rice, 210 gm.
10.04	0.465	0.445	—0.020	Rice, 210 gm.
12.54	0.578	0.530	—0.038	Whole-wheat bread, 450 gm.
13.25	0.617	0.469	—0.148	
12.33	0.635	0.508	—0.147	
15.09	0.755	0.639	—0.116	Mixed diet.
12.00	0.444	1.110	+0.666	5 gm. $NaHCO_3$
11.10	0.444	1.180	+0.726	10 gm. $NaHCO_3$
10.68	0.449	1.430	+0.981	15 gm. $NaHCO_3$
10.75	0.493	0.921	+0.528	Rice, 210 gm.
10.12	0.420	0.521	+0.101	Rice, 210 gm.
11.04	0.456	0.676	+0.220	Rice, 210 gm.
11.10	0.429	0.410	—0.019	Rice, 210 gm.
—and Raisins				
10.06	0.443	0.922	+0.479	Oranges, 800 gm.
10.57	0.495	1.050	+0.555	Oranges, 800 gm.
10.67	0.482	0.692	+0.210	Oranges, 800 gm.
10.46	0.553	0.887	+0.334	Oranges, 1,300 gm.
9.08	0.531	0.670	+0.139	Raisins, 300 gm.
8.62	0.467	0.995	+0.528	Raisins, 300 gm.
8.23	0.450	0.875	+0.420	Raisins, 300 gm.
8.04	0.437	1.310	+0.873	Raisins, 300 gm.
8.57	0.442	0.764	+0.322	Raisins, 300 gm.
10.80	0.510	1.060	+0.550	Oranges, 800 gm.
10.41	0.478	1.060	+0.562	Oranges, 800 gm.
10.41	0.438	0.790	+0.352	Oranges, 800 gm.
10.38	0.443	0.961	+0.518	Oranges, 1,300 gm.
9.24	0.448	0.880	+0.432	Raisins, 300 gm.
8.80	0.425	0.828	+0.403	Raisins, 300 gm.
8.48	0.395	0.832	+0.437	Raisins, 300 gm.
9.01	0.450	1.230	+0.780	Raisins, 300 gm.
7.45	0.383	0.692	+0.309	Raisins, 300 gm.

in the thermostat, through a dried and weighed filter. Both flask and filter are removed from the thermostat and washed thoroughly with cold water. The flask and filter are dried and weighed. The difference between the first and last weighings indicates the amount that has been dissolved. The method is tedious and not without liability to errors. The excess of uric acid might offer opportunity for absorption of urine. The large positive values for the solubility of uric acid obtained by this investigator, however, leave no doubt as to the occurrence of the phenomenon.

OTHER METHODS

The methods for the estimation of titratable acidity and ammonia were those of Folin. Total nitrogen was determined by the Kjeldahl method.

PLAN OF EXPERIMENTS

The subjects were given a uniform diet consisting of 100 gm. graham crackers, 25 gm. dairy-butter and 400 c.c. whole milk at each of the three daily meals. For the evening meal, one soft-boiled egg and a raw apple were added. The latter articles serve a very useful purpose in relieving the relative blandness of the diet. In some cases, when more nitrogen was desired, 10 or 20 gm. of peanut-butter was given at each meal. This ration is ample for protein and energy requirements. No restriction was placed on the amount of water or salt consumed. When data for this basal diet had been established, the effect of the addition of the food in question was studied. Liberal amounts were given, so as to leave no doubt in regard to the interpretation of the results. Whenever possible, the food was eaten in the natural, uncooked state. With such a plan it is not difficult to determine the influence of any food on the composition of the urine. The body quickly reacts to the change, and the new equilibria will generally have been established by the second day. The effect of each food was studied for several days. Somewhat less than a week is sufficient to obtain conclusive data.

Twenty-four-hour specimens of urine were collected, toluene being used as a preservative. The experimental day ended just before breakfast. Analyses were always made as soon as possible after the samples were completed.

The subjects were healthy young men who recognized the need of care in the collection of specimens. No restrictions were placed on them beyond that of diet.

EXPERIMENTAL DATA

SERIES I

Basal Diet (Table 2).—The choice of the diet just described was very fortunate, since it yielded urines which were practically neutral

in reaction, thus making more evident any changes produced by the experimental foods. The average H^+ for the period of six days was 7.31 for Subject W and 7.24 for Subject B, giving a mean value of 7.28. This corresponds very well with the figure (7.34) obtained by Howe and Hawk,[12] using the gas-chain method under similar experimental conditions. It is indeed interesting to note the close agreement in results obtained by the indicator and gas-chain procedures. The values for ammonia N were very constant in both cases, varying with Subject W from 0.224 to 0.287 gm. and with Subject B from 0.234 to 0.323 gm. per day. The uric acid excretion showed typical endogenous figures, the diet being practically purin-free. It will be observed that in these urines the value for the "total solvent power" for uric acid was not greatly different from the amount excreted; that is, in some cases solution took place and in others precipitation occurred. Since these urines were practically neutral, this fact led us to believe that the extent of the solution of uric acid in urine is dependent on H^+. As will appear later, further data supported this conclusion.

Potatoes (Table 3).—The addition of baked potatoes to the basal ration produced a decrease in H^+, as was anticipated because of the excess of basic elements in the ash (Table 1). The value in both cases was 7.74. Ammonia N remained about the same as with the basal diet in the case of Subject W, but was decreased slightly in that of the other subject. The most interesting change brought about was in the "total solvent power" for uric acid, when in every instance, solution of added uric acid took place, the maximum value being 1.23 gm. and the minimum 0.158 gm. It is interesting to note that an increased capacity for the solution of uric acid was associated with a decrease in H^+.

Administration of Alkali, Rice, Wheat Bread, and a Mixed Diet (Table 5).—Varying amounts of sodium bicarbonate were introduced, ranging from 5 gm. on the first day to 10 gm. on the second and 15 gm. on the third day. It was taken by mouth in three equal portions, before meals. In both subjects, there was a gradually decreasing H^+, accompanied by a decreasing ammonia output and by an increasing solvent power for uric acid. On the third day, Subject W excreted only 0.047 gm. of ammonia N, in contrast with his normal output of about 0.2 gm. This clearly illustrates the ability of ingested base to curb ammonia production. The lowest H^+ (8.35) came on the third day, when the bicarbonate intake was the greatest.

12. Howe and Hawk: Proc. Amer. Soc. Biol. Chem., Jour. Biol. Chem., 1914, xvii, 48.

TABLE 7.—NEW—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H⁺]	Ammonia N, gm.
SUBJECT B					
July					
9	1,320	1.015	370	5.70	0.317
10	1,040	1.020	458	5.70	0.412
12	1,475	1.013	560	5.85	0.434
13	620	1.028	518	5.30	0.550
14	940	1.017	466	5.30	0.608
SUBJECT I					
July					
9	975	1.020	429	5.70	0.445
10	1,715	1.013	460	5.70	0.504
12	1,250	1.014	475	5.30	0.495
13	1,310	1.012	482	5.30	0.573
14	1,590	1.011	483	5.50	0.553

TABLE 8.—

SUBJECT B					
July					
15	1,285	1.015	570	5.30	0.602
16	1,700	1.012	578	5.30	0.705
17	710	1.025	540	5.30	0.630
19	1,520	1.016	578	4.80	0.729
SUBJECT I					
July					
15	1,410	1.013	524	5.30	0.559
16	1,610	1.011	537	5.30	0.522
17	1,715	1.010	548	5.30	0.597
19	1,325	1.015	551	4.80	0.635

TABLE 9.—

SUBJECT B					
August					
23	1,880	1.011	376	5.70	0.452
24	915	1.023	476	5.30	0.560
25	830	1.025	604	5.30	0.708
26	985	1.021	614	5.10	0.568
27	1,040	1.020	600	5.30	0.588
28	930	1.023	554	5.30	0.447
SUBJECT I					
August					
23	1,120	1.015	363	5.50	0.417
24	1,290	1.016	469	5.30	0.558
25	1,165	1.016	519	4.90	0.643
26	845	1.020	524	5.10	0.538
27	870	1.019	490	5.10	0.564
28	940	1.017	481	5.30	0.463

—Basal Diet

Total N, gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
7.68	0.472	.....	.....	Basal diet. Whole-wheat crackers, 100 gm.; whole milk, 400 c.c.; dairy-butter, 25 gm. each meal. One soft-boiled egg and one raw apple at supper.
8.46	0.510	0.373	—0.137	
8.85	0.495	0.470	—0.025	
8.33	0.508	0.121	—0.387	
9.42	0.445	0.262	—0.183	
9.00	0.336	.....	.....	Basal diet. Whole-wheat crackers, 75 gm.; whole milk, 400 c.c.; dairy-butter, 25 gm. each meal. One soft-boiled egg and one raw apple at supper.
8.95	0.340	0.070	—0.270	
8.85	0.302	0.093	—0.209	
8.95	0.288	0.069	—0.219	
9.45	0.320	0.077	—0.243	

—Prunes

9.43	0.453	0.105	—0.352	Prunes 330 gm. a day.
9.49	0.434	0.115	—0.319	
7.77	0.396	0.138	—0.258	Prunes, 330 gm. a day.
7.21	0.417	0.113	—0.304	Prunes, 550 gm. a day.
8.90	0.268	0.068	—0.200	Prunes, 240 gm. a day.
9.28	0.238	0.071	—0.167	
9.06	0.318	0.084	—0.234	Prunes, 240 gm. a day.
7.67	0.269	0.071	—0.198	Prunes, 330 gm. a day.

—Plums

7.56	0.427	0.348	—0.079	Plums, 200 gm. each meal.
8.00	0.418	0.224	—0.194	
9.61	0.392	0.165	—0.227	
10.29	0.410	0.161	—0.249	
10.62	0.437	0.199	—0.238	
10.00	0.418	0.157	—0.261	
6.80	0.335	0.155	—0.180	Plums, 150 gm. each meal.
7.81	0.305	0.093	—0.212	
7.97	0.305	0.100	—0.205	
7.72	0.297	0.112	—0.185	
8.36	0.298	0.136	—0.162	
7.69	0.295	0.130	—0.165	

Rice, being a food with a predominance of acid-forming elements, was introduced immediately after the bicarbonate period, in order to magnify the effects of acid production. A gradual rise in H^+ and ammonia and a decreasing ability for uric acid solution were produced. The effects of this acid food became apparent only slowly, on account of the increased store of alkali caused by the previous bicarbonate ingestion. The urines did not show an acid reaction until the end of three days. The ammonia output increased and smaller amounts of added uric acid were dissolved until, on the fourth day, precipitation occurred, showing the urines to be supersaturated.

Subject B continued the experiment for three days on a diet of whole-wheat bread and a final day on a mixed diet. This change brought an increase in H^+ and ammonia and a uniform, negative solution (precipitation) of uric acid. Reference to Table 5 shows how negative values for uric acid solubility accompany an acid urine. This experiment illustrates well the readiness with which the body responds to changes in diet, in order to maintain the usual neutrality.

Potato Ash (Table 4).—The purpose of this experiment was to determine whether or not the effects produced by the potato diet were directly due to the excess of basic, inorganic elements present.

The potatoes were peeled and ashed. This procedure left a gray residue, which was strongly alkaline and partially soluble in water. Since it was impossible to take this product directly, it was given in capsules and even in this form great discomfort was experienced. Soon after its ingestion, a burning sensation developed in the stomach and persisted for some time thereafter. Quantities of ash corresponding to the weights of baked potatoes eaten in the former experiment were employed, the ash being given in three equal portions.

The data show a close similarity in both cases. The effects produced by the ash were less marked than those caused by equivalent amounts of baked potatoes, but this was probably incident to the relative insolubility of the ash. At no time was such a low H^+ reached; but, after the first day, the uric acid solubility showed uniformly positive values, which were greater than those obtained with the basal diet. Therefore, it seems just to conclude that the effects produced by the ingestion of potatoes are referable to the preponderance of basic elements present.

Oranges and Raisins (Table 6).—In order to secure the greatest possible influence of these foods, extra quantities were eaten between meals. Care was taken to obtain chemically untreated raisins. Very similar results were obtained with both fruits, namely, a low H^+ and ammonia output and a uniformly high capacity for the solution of uric acid. When compared with the basal diet, this experiment shows

effects comparable to those found when sodium bicarbonate was taken, and justifies the opinion that these results are due to the basic content of the foods in question.

SERIES II

Opportunity was afforded, during the summer vacation of 1913, for experimental studies in the physiological laboratory of the Battle Creek Sanitarium. I take pleasure in expressing my appreciation of the many kindnesses extended by Dr. J. H. Kellogg and other members of the staff. I am also deeply indebted to Miss Ada Hunt, who very efficiently supervised the preparation of the various diets.

New Basal Diet (Table 7).—This diet was similar to the first, with the exception that whole-wheat crackers were substituted for the graham crackers. This change brought forth an unexpected result, in that a very acid urine was excreted by both subjects. An H^+ of 5.30 was obtained in the two cases, which value is greater than that of the normal human urine, as observed by Henderson and Palmer[5] (1914). Accompanying this were high values for ammonia excretion, typical figures being 0.553 gm. in the case of Subject I and 0.550 gm. in that of Subject B. All of the urines showed a "negative solubility" of uric acid which was more pronounced with Subject I, in whose case in all specimens over 0.2 gm. of this substance was precipitated. The low endogenous uric acid excretion of Subject I is referable to his small weight.

Prunes (Table 8).—As reference to Table 1 shows that prunes are characterized by their great preponderance in basic elements, it seemed highly probable that they would be an ideal food to overcome the highly acid basal diet. Our surprise was great, therefore, when an increased H^+ and ammonia excretion were observed in both cases. On the last day, when the greatest amount of dried prunes was taken, the H^+ was 4.80 for both subjects. Ammonia N values of 0.635 and 0.729 gm., in the urines of Subjects I and B, respectively, prevailed in contrast with the normal output of about 0.56 gm. The large "negative solubility" of uric acid continued throughout this period. This unforeseen result was made clear only by further work with plums, cranberries and benzoic acid.

Plums (Table 9).—The interesting point in connection with fresh plums was to determine whether or not their influence would be similar to that of prunes (dried plums). It is impossible to eat as much of the fresh plums as of the dried prunes, owing to their difference in moisture content. Marked urinary changes were not observed. While no very definite increase in H^+ and ammonia was found, there was no decrease; and on the third day Subject I showed

TABLE 10.—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H·]	Ammonia N, gm.
SUBJECT B					
July					
20	1,095	1.020	466	5.30	0.513
21	1,920	1.012	338	6.30	0.323
22	1,370	1.017	285	7.38	0.255
23	1,535	1.015	298	7.14	0.240
24	1,525	1.017	250	7.38	0.220
SUBJECT I					
July					
20	1,950	1.010	437	5.70	0.492
21	2,285	1.009	343	6.50	0.356
22	1,700	1.012	265	6.90	0.245
23	1,680	1.012	215	7.38	0.181
24	1,960	1.012	227	7.38	0.188

TABLE 11.—

SUBJECT B					
July					
26	1,205	1.014	347	5.70	0.406
27	725	1.022	473	5.30	0.479
28	810	1.025	395	5.70	0.311
29	775	1.025	388	5.70	0.307
30	705	1.028	457	5.50	0.389
31	635	1.029	485	5.30	0.447
SUBJECT I					
July					
26	940	1.018	369	6.00	0.376
27	950	1.016	433	4.90	0.502
28	780	1.022	418	4.90	0.412
29	755	1.023	390	5.30	0.417
30	890	1.021	434	5.50	0.417
31	770	1.022	462	5.30	0.426

TABLE 12.—VEGETARIAN—

SUBJECT B					
August					
2	1,160	1.013	316	5.70	0.445
3	935	1.014	348	5.30	0.618
4	555	1.029	369	5.30	0.380
5	585	1.028	332	5.50	0.412
6	495	1.031	426	5.30	0.366
7	1,080	1.016	363	5.70	0.402
SUBJECT I					
August					
2	1,015	1.016	313	5.70	0.317
3	810	1.020	211	6.90	0.282
4	650	1.023	231	6.00	0.277
5	640	1.022	279	5.70	0.369
6	770	1.018	311	5.50	0.416
7	885	1.016	280	5.70	0.362

—CANTALOUP

Total N, gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
7.93	0.477	0.316	—0.161	Cantaloup, 260 gm. each meal (one melon).
9.32	0.557	0.598	+0.041	
9.38	0.603	0.426	—0.177	
9.87	0.625	0.600	—0.025	
9.48	0.611	0.690	+0.079	
8.07	0.374	0.095	—0.279	Cantaloup, 295 gm. each meal (one melon).
8.50	0.336	0.449	+0.113	
8.37	0.410	0.594	+0.184	
8.26	0.499	0.766	+0.267	
8.47	0.462	1.006	+0.544	

—DASHEEN FLOUR

7.74	0.455	0.288	—0.167	Dasheen flour, 80 gm. daily.
7.78	0.481	0.144	—0.337	
8.61	0.540	0.303	—0.237	
8.78	0.562	0.332	—0.230	
8.68	0.535	0.168	—0.367	
8.68	0.494	0.126	—0.368	
8.19	0.349	0.288	—0.061	Dasheen flour, 60 gm. daily (sanitarium).
7.44	0.282	0.055	—0.217	
7.68	0.340	0.076	—0.264	
7.90	0.338	0.143	—0.195	
8.03	0.308	0.163	—0.145	
8.13	0.322	0.102	—0.220	

—DIET (SANITARIUM)

6.58	0.551	0.448	—0.103	Vegetarian diet (sanitarium).
5.88	0.432	0.142	—0.290	
6.70	0.764	0.117	—0.647	
6.67	0.508	0.246	—0.262	
6.28	0.600	0.120	—0.480	
6.74	0.620	0 296	—0.324	
6.08	0.396	0.276	—0.120	Vegetarian diet (sanitarium).
5.59	0.460	0.450	—0.010	
5.37	0.392	0.323	—0.069	
5.02	0.380	0.145	—0.235	
5.14	0.388	0.112	—0.276	
5.21	0.425	0.201	—0.224	

a high value of 4.90 for H^+. Constantly high values for ammonia N were found in all cases.

Cantaloup (Table 10).—The outcome of this experiment was one of the most satisfactory that we obtained in the entire series. The cantaloup period began on the day following that in which the highly acid conditions, due to the prunes, were met. The effect of this food is well shown in the case of Subject I, when starting with a H^+ of 4.80 on the last prune-diet day there was a steady decrease until this value became 7.38 on the fourth cantaloup-diet day. Similarly, the ammonia N dropped from 0.635 to 0.181 gm. On the second day, positive values for solution of uric acid appeared and continued throughout the period. Subject B responded in essentially the same manner. The values for H^+ changed from 4.80 to 7.38 on the third day, and the ammonia data show a steady decrease from 0.729 to 0.220 gm. An increased excretion of uric acid, amounting to as much as 0.15 gm., appeared in both cases. The cause for this is uncertain. It is possible that uric acid was held back during the highly acid prune period and was then washed out in the alkaline urines resulting from the cantaloup. Indeed, inspection of the values for uric acid excretion during the prune period shows that these were somewhat below the normal.

Dasheen Flour (Table 11).—The dasheen is a plant which is quite similar to the potato (Young[13]). It is a member of the family *Araceae* and of the genus *Colocasia* and has been introduced into this country by the United States government, from the island of Trinidad and the West Indies. The corms and tubers of these plants are similar to the potato but their content of starch and protein is about one-half higher than in the potato, owing to their smaller percentage of water. Since the fresh tubers were not in season, a dasheen flour was used, which was cooked in the form of a gruel and as muffins. It was impossible to eat more than 80 gm. per day, so that no definite effects were produced.

Vegetarian Diet (*Sanitarium*) (Table 12).—Recognizing the fact that vegetables are characterized by a preponderance of basic elements, we investigated the varied lactovegetarian (sanitarium) diet with the expectation of obtaining a low acid output. The two subjects did not respond as anticipated, although the urines of many normal persons living on the same diet had low acidity. These data will be discussed later. Subject I gave a maximum value of 5.50 for H^+ and a minimum figure of 6.90. His ammonia N output ranged from 0.277 to 0.416 gm., while the uric acid solubilities were in every

13. Young: Bur. Plant. Ind., Circ. 127, U. S. Dept. Agric., 1913.

instance negative. Subject B showed a variation in ammonia N from 0.366 to 0.618 gm. A heavy sediment of uric acid was present on the fifth day, which was hardly to be expected with such a diet. An interesting disclosure was the low output of nitrogen—5.4 gm. daily in the case of Subject I and 6.5 gm. in the other. Both were at liberty to eat all they wished, so these figures may perhaps be taken as fairly representing the normal output of nitrogen of persons living on such dietaries.

Tomatoes (Table 13).—Because of the high water content of tomatoes, it is not easy to eat large enough amounts to cause any profound change. Nevertheless, significant departures from the normal allowed the conclusion that the tomato does cause a decrease in H^+ and ammonia excretion. In the case of Subject I, the H^+ varied from 5.70 to 5.85 and the ammonia N from 0.236 to 0.334 gm., the latter being uniformly lower than the basal diet figures. Subject B on three days gave a H^+ of 6.00 and his ammonia N varied between 0.246 and 0.448 gm. Negative values for solubility of uric acid were constantly found.

Celery (Table 14).—The celery was eaten both in the natural state and in the form of a soup, part of the allowance of milk being used in the preparation of this. No significant changes were observed.

Dates (Table 15).—Considerable annoyance was experienced during this study because of the gastro-intestinal fermentation induced by the dates. This disturbance was so severe that Subject I was compelled to end the experiment after the second day, while Subject B continued two days longer. Reference to the table shows no effects which may be related to this food.

Nut Food (Table 16).—This food, a preparation of peanuts, intended to supplant meats in vegetarian diets, is a concentrated food and when taken in undue amounts is rather difficult to assimilate. In these studies, this product was eaten broiled. Low values for ammonia N, without a significant decrease in H^+, were obtained in both cases. The cause of this anomaly remains unexplained.

Cauliflower (Table 17).—This food was thoroughly cooked in a pressure autoclave. It became very distasteful after the third day, so that the experiment was discontinued. In both instances, the first effects seemed to be a decreased output of acid and ammonia, but these were followed by steadily increasing amounts. Subject I, for example, showed at the start a H^+ of 6.00 and ended with the value 5.50. The corresponding figures for ammonia N were 0.237 and 0.490 gm.

Sodium Bicarbonate (Table 18).—Typical results of the administration of alkali, as such, were again found. Ten gm. of sodium

TABLE 13.—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H⁺]	Ammonia N, gm.
SUBJECT B					
August					
9	705	1.022	226	5.70	0.246
10	660	1.027	451	5.70	0.301
11	2,075	1.010	474	6.00	0.448
12	935	1.022	399	5.70	0.281
13	1,030	1.020	346	6.00	0.247
14	870	1.023	381	6.00	0.272
SUBJECT I					
August					
9	625	1.022	275	5.70	0.236
10	890	1.020	427	5.70	0.246
11	1,420	1.012	426	5.70	0.307
12	840	1.020	360	5.85	0.252
13	840	1.020	363	5.70	0.322
14	870	1.020	378	5.70	0.334

TABLE 14.—

SUBJECT B					
August					
16	920	1.020	368	5.70	0.326
17	730	1.026	473	5.30	0.368
18	875	1.028	514	5.50	0.368
19	830	1.030	534	5.30	0.388
20	690	1.029	466	5.30	0.389
21	810	1.029	466	5.30	0.379
SUBJECT I					
August					
16	715	1.023	412	5.30	0.378
17	780	1.024	452	5.30	0.450
18	775	1.026	412	5.50	0.381
19	830	1.024	441	5.30	0.468
20	630	1.024	406	5.30	0.443
21	700	1.024	423	5.30	0.420

TABLE 15.—

SUBJECT B					
August					
30	1,250	1.017	400	5.30	0.405
31	780	1.026	455	5.30	0.403
1	740	1.027	468	5.30	0.338
2	750	1.026	435	5.50	0.301
SUBJECT I					
August					
30	1,210	1.019	397	5.30	0.480
31	1,065	1.016	417	5.30	0.428

—Tomatoes

Total N, gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
6.97	0.534	0.454	—0.080	Tomatoes, 300 gm. each meal.
8.67	0.597	0.170	—0.427	
10.81	0.644	0.457	—0.187	
9.69	0.575	0.489	—0.086	
10.41	0.588	0.562	—0.026	
9.94	0.572	0.455	—0.117	
5.23	0.312	0.245	—0.067	Tomatoes, 200 gm. each meal.
7.64	0.336	0.206	—0.130	
8.14	0.335	0.276	—0.059	
7.56	0.366	0.315	—0.051	
8.52	0.338	0.232	—0.106	
8.47	0.298	0.218	—0.080	
—Celery				
9.39	0.541	0.451	—0.090	Celery, 150 gm. each meal.
8.73	0.528	0.192	—0.336	
10.47	0.585	0.260	—0.325	
10.80	0.594	0.171	—0.423	
9.52	0.475	0.118	—0.357	
10.02	0.525	0.188	—0.337	
8.06	0.302	0.159	—0.143	Celery, 100 gm. each meal.
7.80	0.376	0.169	—0.207	
8.17	0.328	0.167	—0.161	
8.62	0.310	0.087	—0.223	
7.48	0.346	0.113	—0.223	
8.43	0.377	0.108	—0.269	
—Dates				
8.27	0.577	0.313	—0.264	Dates, 150 gm. each meal.
7.68	0.503	0.201	—0.302	
7.86	0.453	0.169	—0.284	
8.20	0.447	0.200	—0.227	
7.91	0.397	0.139	—0.258	Dates, 100 gm. each meal.
6.78	0.272	0.087	—0.183	

bicarbonate daily gave a H^+ of 7.38 in the case of Subject I and of 6.70 in that of Subject B, while 15 gm. caused a further reduction to 8.00 in both cases. Another very low excretion of ammonia N was observed in Subject I on the second day, when only 0.072 gm. was excreted. Uric acid showed practically no tendency to precipitate; indeed, in the case of Subject I the values for the excretion and

TABLE 16.—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H⁺]	N, gm. Ammonia
SUBJECT B					
September					
9	1,130	1.022	427	5.70	0.244
10	950	1.027	502	5.70	0.285
11	1,030	1.025	494	5.70	0.241
SUBJECT I					
September					
9	890	1.024	392	5.70	0.235
10	745	1.024	465	5.30	0.277
11	950	1.023	460	5.50	0.239

TABLE 17.—

SUBJECT B					
September					
13	1,830	1.016	380	6.00	0.362
14	1,020	1.026	563	5.50	0.515
15	1,450	1.018	609	5.50	0.697
SUBJECT I					
September					
13	1,040	1.020	316	6.00	0.237
14	1,300	1.017	354	6.00	0.328
15	1,020	1.020	465	5.50	0.490

TABLE 18.—SODIUM—

SUBJECT B					
September					
16	1,270	1.015	335	6.70	0.305
17	1,950	1.012	226	8.00	0.140
SUBJECT I					
September					
16	820	1.019	256	7.38	0.256
17	1,200	1.017	154	8.00	0.072

"total solvent power" were identical. Circumstances made it impossible to carry out these determinations on the second experimental day.

SERIES III

Basal Diet (Table 19).—The original basal diet of graham crackers, whole milk, dairy-butter and peanut-butter was used for the

remaining experiments in New Haven. Here again is noticed the approximate neutrality of urines resulting from this diet. The average H^+ of all the urines of the four subjects, during a period of five days, was 7.10, or a slight alkalinity. Corresponding to this value were comparatively low figures for ammonia N, Subjects H and M excreting greater amounts than did the two others, on account of

—Nut Food

Total N, gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
11.53	0.579	0.405	—0.174	Nut food, 100 gm. each meal.
12.38	0.593	0.206	—0.387	
13.63	0.598	0.321	—0.277	
9.64	0.356	0.271	—0.085	Nut food, 100 gm. each meal.
9.97	0.330	0.111	—0.219	
11.52	0.416	0.198	—0.218	
—Cauliflower				
11.10	0.651	0.596	—0.055	Cauliflower, 150 gm. each meal.
12.34	0.744	0.191	—0.553	
13.80	0.720	0.227	—0.493	
8.23	0.456	0.360	—0.096	Cauliflower, 100 gm. each meal.
9.63	0.483	0.386	—0.097	
9.50	0.470	0.117	—0.353	
—Bicarbonate				
11.32	0.535	0.509	—0.026	$NaHCO_3$, 10 gm.
.....	.....	.....	.....	$NaHCO_3$, 15 gm.
7.98	0.363	0.363	+—0.000	$NaHCO_3$, 10 gm.
.....	.....	.....	.....	$NaHCO_3$, 15 gm.

their higher nitrogen intake. Uric acid solubility was determined only in the urines of Subject W. The previously observed phenomenon of occasional precipitation was found to hold for these practically neutral urines.

Bananas (Table 20).—The influence of this food is clearly exhibited in the case of Subject W, whose urines gave a uniform value of

7.43 for H^+ throughout, as against an average of 7.19 on the basal diet. The ammonia N dropped from an original value of over 0.2 gm. to an average of about 0.15 gm. daily. The most striking observation was in the change of solubility of uric acid from practically zero to a positive value of 0.4 gm. dissolved. The same effects were observed in the case of Subject M.

Apples (Table 21).—Two large raw apples, besides the usual one at supper, were eaten with meals, the skins not being discarded. A decrease in H^+ was found in both instances. The average H^+ of Subject B on the basal diet (6.86) became 7.38 under the influence of apples, while the corresponding values for Subject H were 7.24 and 7.43. A small but irregular decrease in ammonia N was observed in both cases.

Benzoic Acid (Table 22).—It will be recalled that plums and prunes caused an increased acid excretion, which was contrary to the theoretical deductions from the ash analyses. The most plausible explanation is that these fruits contain some substance which is non-combustible in the body and is excreted in the form of a relatively strong acid. Benzoic acid, which is found in prunes to the extent of 0.05 per cent. (Radin[14]), is excreted as hippuric acid.

To determine the effect of benzoic acid on urinary acidity, 1 gm. in a capsule was taken before each meal. At no time were any ill effects noticed by any of the three subjects. The results of the acid ingestion are well illustrated by Subject W, who showed an increase in H^+, which reached 5.30 and was at no time less than 6.30. Paralleling this was an average daily output of ammonia N of 0.392 gm., as against 0.242 gm. with the basal diet. Likewise, negative solution (precipitation) of uric acid obtained in all the urines. Comparable effects were shown by Subjects B and M.

An increased acid production due to the ingestion of benzoic acid is not hard to explain, since it is well known that from it the kidneys synthesize hippuric acid, the strongest of the urinary acids. Judging from previous experience, the augmented ammonia formation which accompanied this increased acid elimination was to be expected. These results are not in harmony with those obtained with pigs by M'Collum and Hoagland,[5] who reported absence of an increase in ammonia when benzoic acid was fed. Their tables, however, show a noticeable increase in this factor.

Further evidence that benzoic acid ingestion increases the acidity is revealed in the different studies made on urinary antiseptics, such as hexamethylenetetramin, which requires an acid reaction before for-

14. Radin: Unpublished data from this laboratory, 1914.
15. M'Collum and Hoagland: Jour. Biol. Chem., 1913, xvi, 321.

maldehyd can be liberated from it. Walker[16] and Jordan[17] have demonstrated that benzoic acid and ammonium benzoate are efficient in bringing about the requisite acid condition.

Cranberries (Table 23).—These berries have long been the classic example of a natural food containing benzoic acid. Their content of this acid is 0.06 per cent. (Radin).[14] In view of the interesting disclosures resulting from the preceding experiment, we deemed it worth while to include this food in our study. The berries were taken in the familiar form as a sauce. No discomfort was observed even when the original amount of 300 gm. of sauce daily was increased to 600 gm. on the sixth day. Large quantities of fecal matter were passed, which probably explains the diminished excretion of urinary N encountered in the latter days of the experiment.

The data obtained from Subject W may be taken as truly representative of the conditions prevailing in all four subjects. On the last day of greatest cranberry intake, a H^+ of 5.70 was found and the corresponding value for ammonia N was 0.346 gm., both being marked increases over those obtained with the basal diet. Negative values for solubility of uric acid were exhibited by all the urines. The unanimity of results obtaining for these four subjects justifies the belief that the acid production following cranberry-eating is caused by their content of benzoic acid.

The H^+ of the Urines of Thirty Vegetarians (Table 24).—Unusual opportunity was at hand for obtaining urines of persons who had lived on a vegetarian diet for varying lengths of time, some having been exclusive vegetarians for twenty-five years. The subjects were physicians, nurses, bath-room attendants and helpers about the Battle Creek Sanitarium. All were required to turn in a written report of their diet and were carefully instructed regarding the collection of samples. The twenty-four-hour specimens were preserved with toluene. The thirty samples were from as many persons, both men and women. Reference to the table shows a range in H^+ from 5.30 to 7.48, with an average value of 6.64, which is somewhat less than that of 5.98 reported by Henderson and Palmer[5] for normal human urine. Doubtless, their observations were made on individuals living on an ordinary mixed diet. The diet lists of those persons who produced alkaline urines showed that they were eating heartily of potatoes and cantaloup, both of which are efficient in decreasing acid formation. It is reasonable to expect that a vegetarian diet, with its preponderance in basic elements, will cause the production of a less acid urine than will a mixed diet in which the meats, with their surplus of acid-

16. Walker: Brit. Med. Jour., 1913, ii, 643.
17. Jordan: Brit. Med. Jour., 1913, ii, 654.

TABLE 19.—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H⁺]	Ammonia N, gm.
SUBJECT B					
October					
19	1,090	1.016	305	6.70	0.282
20	1,290	1.015	325	6.90	0.248
21	1,310	1.013	346	6.90	0.251
22	1,460	1.014	374	6.90	0.245
23	1,200	1.016	338	6.90	0.216
SUBJECT H					
October					
19	1,010	1.016	258	6.90	0.303
20	1,200	1.018	273	7.38	0.382
21	2,040	1.011	302	7.38	0.539
22	1,050	1.019	323	7.38	0.346
23	1,455	1.015	352	7.14	0.412
SUBJECT M					
October					
19	1,355	1.014	311	6.90	0.521
20	2,180	1.011	305	7.43	0.314
21	1,060	1.020	369	7.38	0.465
22	940	1.022	363	6.90	0.502
23	1,060	1.019	377	6.90	0.413
SUBJECT W					
October					
19	945	1.019	340	6.90	0.284
20	1,030	1.020	359	7.38	0.204
21	1,350	1.017	367	7.38	0.268
22	1,170	1.019	393	7.14	0.239
23	1,000	1.021	408	7.14	0.216

TABLE 20.—

SUBJECT M					
October					
31	1,600	1.015	301	7.48	0.288
1	1,230	1.021	271	7.43	0.332
2	1,460	1.015	257	7.48	0.289
3	1,190	1.017	257	7.43	0.315
4	1,400	1.015	185	7.43	0.269
SUBJECT W					
October					
31	1,450	1.015	296	7.43	0.148
1	1,250	1.018	240	7.43	0.157
2	1,330	1.016	293	7.43	0.144
3	1,260	1.018	282	7.43	0.121
4	1,360	1.016	223	7.43	0.139

—Basal Diet

Total N, gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
9.82	.....	.....	.....	Basal diet. 100 gm. Graham crackers; whole milk, 1 pint; dairy-butter, 25 gm., each meal. One soft-boiled egg and one raw apple extra for supper.
10.22	.....	.....	.....	
10.29	.....	.....	.....	
10.12	.....	.....	.....	
10.65	.....	.....	.....	
9.71	.....	.....	.....	Basal diet. Graham crackers, 100 gm.; whole milk, 1 pint; dairy-butter, 25 gm.; peanut-butter, 20 gm. These were taken each meal. At supper one soft-boiled egg and one raw apple.
12.20	.....	.....	.....	
13.22	.....	.....	.....	
10.83	.....	.....	.....	
13.31	.....	.....	.....	
11.58	.....	.....	.....	Basal diet. Graham crackers, 100 gm.; whole milk, 1 pint; dairy-butter, 25 gm., and peanut-butter, 20 gm. each meal. One soft-boiled egg and one raw apple extra for supper.
13.34	.....	.....	.....	
11.58	.....	.....	.....	
12.85	.....	.....	.....	
12.24	.....	.....	.....	
10.54	.....	.....	.....	Basal diet. Graham crackers, 100 gm.; whole milk, 1 pint; dairy-butter, 25 gm., and peanut-butter, 10 gm. each meal. One soft-boiled egg and one raw apple extra at supper.
11.00	0.381	0.369	—0.012	
11.78	0.391	0.610	+0.219	
11.68	0.400	0.112	—0.288	
11.85	0.393	0.382	—0.011	

—Bananas

12.34	.....	.....	.....	Bananas, about 310 gm. each meal.
10.12	.....	.....	.....	
11.53	.....	.....	.....	
9.71	.....	.....	.....	
10.34	.....	.....	.....	
9.88	0.393	0.873	+0.480	Bananas, about 310 gm. each meal.
10.60	0.398	0.841	+0.443	
10.27	0.370	0.752	+0.382	
10.62	0.378	0.779	+0.401	
10.13	0.410	0.973	+0.563	

forming elements, constitutes a significant part. Nevertheless, the fact must not be forgotten that a vegetarian diet, if it is composed largely of the cereals, may be just as acidic or even more than a mixed diet.

TABLE 21.—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	[H·]	Ammonia N, gm.
SUBJECT B					
October					
31	1,720	1.010	407	6.90	0.320
1	2,110	1.008	279	7.38	0.190
2	1,760	1.010	359	7.38	0.306
3	1,810	1.010	304	7.38	0.239
4	2,110	1.009	295	7.43	0.190
SUBJECT H					
October					
31	2,300	1.008	239	7.38	0.372
1	1,870	1.011	292	7.43	0.337
2	1,510	1.014	278	7.43	0.389
3	1,750	1.012	266	7.43	0.357
4	1,670	1.012	294	7.43	0.350

TABLE 22.—

SUBJECT B					
October					
24	1,620	1.011	392	6.15	0.292
26	1,640	1.013	410	6.15	0.374
27	1,600	1.013	443	6.00	0.422
28	1,620	1.013	434	6.00	0.408
29	1,340	1.015	468	5.70	0.418
SUBJECT M					
October					
24	1,250	1.018	325	6.70	0.428
26	1,660	1.013	382	6.70	0.678
27	1,850	1.013	437	6.70	0.600
28	1,175	1.020	470	6.30	0.628
29	1,370	1.017	420	6.70	0.608
SUBJECT W					
October					
24	930	1.022	458	6.30	0.302
26	1,480	1.014	435	6.00	0.400
27	1,060	1.021	518	5.70	0.438
28	1,320	1.017	470	5.70	0.388
29	1,090	1.020	538	5.30	0.432

H^+ ion Concentration and the Carbon-Dioxid Tension of the Alveolar Air (Table 25).—The determination of the tension of alveolar CO_2 has recently come into prominence as a diagnostic measure in cases of acidosis. It is particularly useful in advanced cases of

diabetes. In these, the tension of CO_2 is always lower than normal. This lowered value is attributed to a diminished alkalinity of the blood, which decreases the CO_2 in the blood and, therefore, the tension of this gas in the pulmonary alveoli.

Total N. gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
—Apples				
8.37	.....	.....	.....	Two apples extra each meal. About 2,300 gm. daily.
7.67	.....	.....	.....	
9.24	.....	.....	.....	
8.53	.....	.....	.....	
8.85	.....	.....	.....	
9.26	.....	.....	.....	Two apples extra with each meal, about 2,300 gm. daily.
10.99	.....	.....	.....	
10.33	.....	.....	.....	
11.66	.....	.....	.....	
10.63	.....	.....	.....	
—Benzoic Acid				
10.84	.....	.....	.....	Benzoic acid, 1 gm., in a capsule before each meal.
9.94	.....	.....	.....	
9.76	.....	.....	.....	
10.46	.....	.....	.....	
10.59	.....	.....	.....	
13.06	.....	.....	.....	Benzoic acid, 1 gm., before each meal.
12.44	.....	.....	.....	
12.38	.....	.....	.....	
12.34	.....	.....	.....	
13.00	.....	.....	.....	
11.38	0.385	0.216	—0.169	Benzoic acid, 1 gm., before each meal.
10.83	0.367	0.256	—0.111	
10.97	0.385	0.156	—0.229	
11.32	0.402	0.222	—0.180	
10.49	0.350	0.063	—0.287	

It seemed desirable to discover the behavior of the H^+ of the urine in connection with the alveolar CO_2 tension and to establish a relationship, if possible. The Haldane[18] method was used in the determin-

18. Haldane and Priestly: Jour. Physiol., 1905, xxxii, 225.

ations of the alveolar CO_2 tension.[19] The samples were always taken at the same hour, before breakfast. The subjects sat in an easy position for at least five minutes before the air was collected. Triplicate estimations of the air taken at the end of a forced expiration, following normal inspiration, were always made. Unfortunately, during this series of trials only one diet (cantaloup) caused the production of an alkaline urine. Reference to Table 25 shows that, during the prune period, Subject B had a CO_2 tension of 34 mm. with a H^+ of 5.30. Under the influence of the cantaloups, the CO_2 tension increased to a maximum of 38.2 mm. and the H^+ decreased to 7.38. On returning to the acid diet, a drop in CO_2 tension was observed. At no time during the remainder of the experiment were these high values for CO_2 tension of the cantaloup diet again reached. The ingestion of 15 gm. sodium bicarbonate, daily, produced a tension of CO_2 of 36.7 mm. and a H^+ of 8.00. The other subject responded in a similar manner, although the values obtained were not so uniform. The breathing of this subject was very shallow, which made the collection of the samples of air difficult. It will be observed that Subject B had a lower CO_2 tension than normal. This is probably explained by his habitually deep respirations, which allowed of more complete ventilation.

The change in CO_2 tension appears more quickly than does that in the H^+ of the urine. Thus, on the last prune-diet day Subject B gave a CO_2 tension of 34.09 mm., which became 37.0 mm. on the first day on cantaloups. The corresponding variations in H^+ were only slight, from 4.80 to 5.30. It was to be expected that the blood would respond more quickly, because of its great power of maintaining a constant reaction.

Hasselbalch[20] (1912) has reported similar changes brought about by variations in diet. The values for CO_2 tension obtained with one of this author's subjects were as follows; meat diet 37.8 mm., mixed diet 38.3 mm., vegetarian diet 43.3 mm., and alkaline diet ($NaHCO_3$) 42.1 mm. Hasselbalch says:

> A diet which produces an acid urine causes a low carbon dioxid tension of the blood; a diet that produces a less acid or an alkaline urine causes at the same time a high carbon dioxid tension of the blood.[21]

H. Straub[22] has stated that these changes in the CO_2 tension of alveolar aid produced by diet are only temporary. He is of the

19. These estimations were made by Dr. Paul Roth of the Battle Creek Sanitarium.

20. Hasselbalch: Biochem. Ztschr., 1912, xlvi, 403.

21. Eine Diät, die einen sauren Harn verursacht, bewirkt eine niedrige CO_2-Spannung des Blutes; eine Diät, die einen weniger sauren oder alkalischen Harn verursacht, bewirkt gleichzeitig eine hohe CO_2-Spannung.

22. Straub, H.: Deutsch. Arch. f. klin. Med., 1913, cix, 223.

opinion that the CO_2 tension soon returns to normal, and may even be normal in cases of diabetes, provided the acidosis is not too great.

The H^+ of blood at different pressures of CO_2 has been studied by Hasselbalch and Lundsgaard[23] (1911). They found that, at a pressure of about 40 mm. CO_2, a change of 1 mm. of CO_2 pressure made a difference of only 0.0065 times 10^{-7} in the H^+ of the blood. It has been shown by Campbell, Douglas, Haldane and Hobson[24] (1913) that a difference of about 0.8 mm. in the normal tension of alveolar CO_2 of 40 mm. gives an increase of 50 per cent. in the alveolar ventilation. This corresponds to a change in H^+ of only 0.005 times 10^{-7}. From this it becomes evident that the respiratory center, during normal life, responds to very minute changes in the H^+ of the blood. Since the CO_2 tension of alveolar air remains remarkably constant, it is plain that the chief regulation of the H^+ of the blood takes place in other organs besides the lungs. All evidence points to the kidneys as exerting the greatest rôle in the maintenance of this constancy in reaction.

Higgins[25] (1914) has very recently reported observations which indicate that some other factor besides the H^+ of the blood is acting on the respiratory center. He finds that the alveolar CO_2 tension is markedly influenced by posture, being higher when the subject is standing than sitting and higher when sitting than lying. It was also noted that beefsteak and sugar ingestion produced an increased CO_2 tension, lasting as long as the food was being absorbed. Coffee drinking caused a decrease in the CO_2 tension of alveolar air. From this author's experience, there is reason to believe that a high CO_2 tension of alveolar air is associated with vasodilatation, and a low alveolar CO_2 tension with vasoconstriction.

DISCUSSION

When the preceding results are carefully observed, it readily becomes apparent that urinary acidity, the output of ammonia and the solvent power for uric acid can be materially changed by appropriate variations in diet. It has been my purpose to show that these changes are referable to the character of the ash yielded by the several foods, so far as this represents likewise the end-result of the oxidation of the nutrients in the organism. In this respect, the foods or diets may be said to possess a potential acidity or alkalinity. The possibility of the presence of certain organic substances which are excreted as acids must be taken into account; for example, benzoic acid. In general, the results obtained have been those which were

23. Hasselbalch and Lundsgaard: Biochem. Ztschr., 1911, xxxviii, 77.
24. Campbell, Douglas, Haldane and Hobson: Jour. Physiol., 1913, xlvi, 301.
25. Higgins: Am. Jour. Physiol., 1914, xxxiv, 114.

expected. Thus, foods which yield an alkaline ash decrease the urinary acidity, while those yielding an acid-reacting residue increase this factor. In order to make more clear the relations existing between the different urinary factors, they will be considered from various points of view.

TABLE 23.—

Date 1913	Volume c.c.	Specific Gravity	Acidity N/10, c.c.	$[H^+]$	Ammonia N, gm.
SUBJECT B					
November					
6	1,000	1.018	413	6.15	0.264
7	1,255	1.014	391	6.30	0.219
8	1,460	1.012	356	6.30	0.280
9	1,500	1.013	354	6.70	0.288
10	1,600	1.014	423	6.30	0.269
11	1,090	1.016	432	5.85	0.380
12	1,230	1.015	488	5.70	0.391
SUBJECT H					
November					
6	865	1.021	291	6.70	0.462
7	830	1.021	462	6.30	0.537
8	1,890	1.013	492	6.70	0.601
9	965	1.019	355	6.70	0.394
10	960	1.021	346	6.70	0.444
11	1,060	1.019	373	6.70	0.534
12	1,630	1.012	359	6.70	0.528
SUBJECT M					
November					
6	1,060	1.018	403	6.90	0.522
7	1,215	1.017	379	6.90	0.423
9	1,630	1.011	372	6.90	0.431
10	1,520	1.014	322	6.90	0.383
11	1,510	1.015	387	6.90	0.734
12	825	1.024	419	6.30	0.610
SUBJECT W					
November					
6	985	1.021	422	6.50	0.237
7	915	1.021	403	6.50	0.198
8	1,030	1.019	470	6.00	0.303
9	880	1.022	359	6.70	0.253
10	1,030	1.020	446	6.00	0.266
11	1,280	1.016	451	6.00	0.330
12	960	.....	442	5.70	0.346

THE RELATION OF H^+ TO TITRATABLE ACIDITY

Determinations of the excess of acid over basic radicals were made along with estimations of the true acidity or the H^+ ion concentration. Our results agree with those very recently reported by Henderson and Palmer,[5] who reached the conclusion that titratable acidity

is a function of the H^+. Thus, they found that the average values of A (titratable acidity) steadily diminished from 320 c.c. N/10 NaOH with a H^+ of 5.4 to 224 c.c. with a H^+ of 6.6. It is their belief that in the more acid specimens the variations in acidity are dependent on variations in the manner of the treatment of constant amounts of

—CRANBERRIES

Total N, gm.	Uric Acid, gm.	Solubility of Uric Acid		Diet
		Total gm.	Residual gm.	
10.24	.....	.....	.....	Cranberry-sauce, 100 gm., each meal.
9.34	.....	.....	.....	
9.24	.....	.....	.....	
9.82	.....	.....	.....	
9.55	.....	.....	.....	
8.86	.....	.....	.....	Cranberry-sauce, 200 gm., each meal.
8.24	.....	.....	.....	
10.45	.....	.....	.....	Cranberry-sauce, 100 gm., each meal.
10.52	.....	.....	.....	
14.03	.....	.....	.....	
9.53	.....	.....	.....	
10.21	.....	.....	.....	
10.02	.....	.....	.....	Cranberry-sauce, 200 gm., each meal.
9.89	.....	.....	.....	
9.87	.....	.....	.....	Cranberry-sauce, 100 gm., each meal.
11.42	.....	.....	.....	
10.48	.....	.....	.....	
10.36	.....	.....	.....	
9.28	.....	.....	.....	Cranberry-sauce, 200 gm., each meal.
7.95	.....	.....	.....	
10.60	0.362	0.293	—0.069	Cranberry-sauce, 100 gm., each meal.
10.52	0.355	0.242	—0.113	
11.10	0.389	0.207	—0.182	
10.13	0.361	0.320	—0.041	
9.72	0.362	0.171	—0.191	
9.38	0.329	0.182	—0.147	Cranberry-sauce, 200 gm., each meal.
8.53	0.292	0.060	—0.232	

phosphoric acid by the regulatory mechanism, and results simply in a change in the proportion of acid to alkaline phosphate in the urine. The following hypotheses are offered by them: (*a*) With a constancy in the excretion of phosphoric acid, the H^+ will vary with A according to the mass law equilibrium of phosphoric acid. (*b*) With a con-

stancy of acid excretion, the H^+ will vary inversely with the phosphate. These investigators believe that in the least acid samples there must have been greater amounts of phosphate excreted. The explanation offered follows: If the amount of phosphate claiming excretion is large and the body does not need to get rid of abnormally great amounts of acid, then it must eliminate a urine low in H^+ in order not to bring about general alkalinity of the body. A glance over our tables shows that the titratable acidity and the H^+ maintain a general relationship. This is well illustrated by the change from the prune to the cantaloup diet (Tables 8 and 10). Subject B on the last prune-diet day gave a H^+ of 4.80 and a value for A of 578 c.c. On the last cantaloup-diet day these became 7.38 and 250 c.c., respectively. Many more examples of this similarity in behavior are disclosed by our data.

TABLE 24.—THE H^+ OF THE URINES OF THIRTY VEGETARIANS

6.90	6.90	6.30
6.00	5.70	7.43
7.43	6.30	7.38
6.30	7.38	6.70
6.30	6.30	5.70
7.48	6.70	5.70
5.30	7.14	5.30
6.90	6.30	7.38
7.43	5.70	6.70
7.43	7.48	7.38

Average, 6.64

THE RELATION OF H^+ TO URINARY AMMONIA

Our results show, almost without exception, that these two factors are intimately related. An increase in H^+ is accompanied with an augmented ammonia production and vice versa. This sequence is well illustrated by the change from the highly acid prune diet to the basic cantaloup diet (Tables 8 and 10). Subject I showed values of 4.80 for H^+ and of 0.635 gm. ammonia N on the last prune-diet day. On the last cantaloup-diet day these were 7.38 and 0.188 gm., respectively. The other subject responded in a like manner. Other cases were observed in which these relationships held; the well-known, exceptionally low values for ammonia N were found after ingestion of alkalies. Examples of an increased ammonia output, with an increase in H^+, were observed in the benzoic acid experiment and in the prune, plum, cranberry and rice studies. These marked changes in ammonia excretion show that this factor plays an important rôle in the preservation of body neutrality. We believe that ammonia plays a greater part in checking the acidity of body fluids than Henderson and Palmer[5] assign to it. They state that their investigations prove conclusively that in normal persons nearly if not quite all the

TABLE 25.—H^+ Ion Concentration and the Carbon Dioxid Tension of the Alveolar Air

Date	Diet	Subject B		Subject I	
		H^+ Urine	CO_2 Tension mm.	H^+ Urine	CO_2 Tension mm.
July					
14	Basal diet	5.30	35.4	5.50	43.6
15	Prunes	5.30	34.0	5.30	39.5
16	Prunes	5.30	33.2	5.30	40.0
17	Prunes	5.30	33.1	5.30	38.9
19	Prunes	4.80	34.1	4.80	39.1
20	Cantaloup	5.30	37.0	5.70	42.8
21	Cantaloup	6.30	36.7	6.50	42.8
22	Cantaloup	7.38	38.2	6.90	43.8
23	Cantaloup	7.14	38.2	7.38	42.0
24	Cantaloup	7.38	37.6	7.38	41.8
26	Dasheen flour...	5.70	35.9	6.00	43.5
27	Dasheen flour...	5.30	35.0	4.90	43.6
28	Dasheen .our...	5.70	35.2	4.90	41.0
29	Dasheen flour...	5.70	35.1	5.30	41.0
30	Dasheen flour...	5.50	35.9	5.50	40.3
31	Dasheen flour...	5.30	32.0	5.30	40.0
Aug.					
2	Vegetarian	5.70	33.6	5.70	41.3
3	Vegetarian	5.30	33.0	6.90	42.3
4	Vegetarian	5.30	31.3	6.00	41.7
5	Vegetarian	5.50	33.2	5.70	41.3
6	Vegetarian	5.30	33.4	5.50	41.2
7	Vegetarian	5.70	33.2	5.70	40.3
9	Tomatoes	5.70	34.0	5.70	40.7
10	Tomatoes	5.70	34.5	5.70	39.9
11	Tomatoes	6.00	32.6	5.70	40.9
12	Tomatoes	5.70	35.0	5.85	39.9
13	Tomatoes	6.00	31.5	5.70	41.0
14	Tomatoes	6.00	32.6	5.70	39.0
16	Celery	5.70	32.6	5.30	40.1
17	Celery	5.30	33.9	5.30	39.4
18	Celery	5.50	31.4	5.50	42.0
19	Celery	5.30	32.0	5.30	41.0
20	Celery	5.30	33.1	5.30	39.7
21	Celery	5.30	32.5	5.30	39.1
23	Plums	5.70	33.0	5.50	42.2
24	Plums	5.30	32.5	5.30	42.1
Sept.					
1	Dates	5.30	34.7	5.30	41.5
2	Dates	5.50	33.3		
9	"Nuttolene"	5.70	35.6	5.70	40.5
10	"Nuttolene"	5.70	33.7	5.30	41.2
11	"Nuttolene"	5.70	32.7	5.50	40.5
13	Cauliflower	6.00	33.1	6.00	42.5
14	Cauliflower	5.50	33.1	6.00	42.7
15	Cauliflower	5.50	32.7	5.50	43.6
16	$NaHCO_3$, 10 g..	6.70	36.7	7.38	43.1
17	$NaHCO_3$, 15 g..	8.00	36.7	8.00	43.5

final regulation of H^+ through excretion falls on the phosphates and that the ammonia does not materially vary for purposes of regulating the reaction of the blood. The importance of the phosphates and bicarbonates in maintaining body neutrality is not minimized by us, but we feel that the significant changes in ammonia excretion observed indicate that this factor exerts a decided influence in this direction.

THE RELATION OF H^+ TO VOLUME

In their most recent publication, Henderson and Palmer[5] have reported an apparent relationship between urine volume and extent of acidity. Their averages showed that, with an increase in volume, there resulted a decrease in titratable and true acidity. While this does hold for their averages, yet a close inspection reveals many individual exceptions among their different cases. Our results do not permit of this conclusion. A good example of the non-relationship of these two is found in the case of Subject B (Table 10). His volume on the second prune-diet day was 1,700 c.c., and on the following day was only 710 c.c., while the H^+ remained the same on both dates. The last day of this period showed a volume of 1,520 c.c. and a higher H^+ of 4.80. Numerous other illustrations of this lack of relationship are to be observed. Our data can hardly allow of the conclusion that has been offered by these investigators. Haskins[26] has also failed to find any relation between the concentration of urine and its acidity. In all experiments on urinary acidity, the food factor must be carefully considered. If this is not done, erroneous conclusions are liable to be drawn.

THE RELATION OF H^+ TO THE SOLUTION OF URIC ACID

Early in this study, a close relationship between H^+ and the extent of solution of uric acid became apparent. The regularity with which urines having a greater H^+ than 7.00 deposit uric acid, while the alkaline urines dissolve this substance, is striking. Very acid urines are greatly supersaturated, as is shown in Tables 7 and 8. On the other hand, the heightened capacity for dissolving uric acid is to be seen in the alkaline urines of Tables 2 and 3. Specimens which are practically neutral in reaction are usually saturated. Such samples will sometimes experience precipitation, while in others solution will take place; but the amount is never large in either direction. The extent of the solution of uric acid in urine appears to be chiefly a function of the H^+. We have been able to confirm the observations of Hindhede and in a measure to explain the nature of this phenomenon. As has been mentioned, this worker found a relationship existing between titratable acidity and the capacity for the solution of uric

26. Haskins: Proc. Am. Chem. Soc., Science, New Series, 1913, xxxviii, 679.

acid. He suggested that since urines derived from diets containing certain vegetables, particularly the potato, were able to bring this substance into solution, the cause of the phenomenon might be found in the character of the ash of these foods. No experimental evidence for this was given. Our data show that such is really the case. Foods with an excess of base-forming elements lead to the production of a less acid urine. If the reduction is enough to result in an alkaline urine, then a heightened capacity for the solution of uric acid is obtained. Hindhede intimated that the volume of the urine might play a part in this phenomenon. Our results indicate that ordinary variations in urine volume exert an insignificant influence. It may well be, however, that this factor enters materially, when such large excretions (from 3 to 4 liters) as were obtained by Hindhede are dealt with.

That urine generally contains more than enough uric acid for saturation is well known. There have been many attempts to determine the factors responsible for this condition. The advent of colloidal chemistry has stimulated some investigators in their efforts to apply it in explanation of the supersaturation of uric acid solutions. Among others, Schade and Boden[27] have been enthusiastic supporters of the colloidal theory. They believe that supersaturated solutions of this substance are made possible by the formation of a uric acid colloid. Recently, however, Kohler[28] has reported experiments which indicate that supersaturated solutions of sodium urate and of uric acid are true solutions and not of a colloidal nature. He arrived at these conclusions by dialyzing a supersaturated solution of sodium urate against a saturated solution. At the end of twenty-four hours, the two solutions were of equal concentration. Furthermore, the electrical conductivity of supersaturated solutions of sodium urate was practically equal to that of unsaturated or saturated solutions. Had the supersaturated solution been of a colloidal nature, its conductivity would have been greatly diminished. This investigator admits the possibility of the colloids being a factor but assigns to them a small part in the phenomenon.

PRACTICAL CONSIDERATIONS

The data presented make it clear that certain vegetables and fruits, on account of their preponderance in basic elements, lead to the formation of less acid urines. In this, their action is comparable to that of sodium bicarbonate and citrate, which are widely used in therapeutics. The question arises, can these efficient fruits and vege-

27. Schade and Boden: Ztschr. f. physiol. Chem., 1913, lxxxiii, 346; ibid., 1913, lxxxvi, 238.
28. Kohler: Ztschr. f. klin. Med., 1913, lxxviii, 205.

tables render similar service in therapy? If the desired ends can be obtained by a proper choice of diet, then a valuable step has been taken. Some of the possible applications of diet are, herewith, presented.

NEPHRITIS

One of the current but much controverted theories of nephritis is that of Fischer.[29] This author believes that all the signs and symptoms of this disease are referable to changes in the condition of the kidney colloids. The cause of the pathological condition, according to Fischer, is an abnormal production or accumulation of acid in the kidney. The presence of acid is said to favor the solution of the kidney colloids; hence the albuminuria. Its action in making the kidney colloids swell is assumed to explain the increase in size of this organ, and further, it precipitates a second colloid making the change in color (graying) of the kidney. That there is an increased amount of urinary acid in nephritis is shown by the work of Henderson and Palmer.[2] These experimenters obtained an average value of 5.33 for the H^+ of the urine of cardiorenal cases, in contrast with the normal figure of 5.98. The work of Lewis, Ryffel, Wolf, Cotton and Barcroft[30] shows that in cardiorenal cases there is often a marked acidosis, with an accompanying fall in the CO_2 tension of the alveolar air.

If this acid theory of nephritis is true, then the treatment indicated is the introduction of bases in order to overcome this increased acidity. Fischer[31] has reported much success in the treatment of nephritics by alkalies. That patients with kidney lesions differ in their response to the administration of alkalies has been shown by Palmer.[32] He reports that it is difficult to reduce urinary acidity in many nephritics by alkaline treatment, but that after the urine has been rendered alkaline and then allowed to become acid, the patients respond normally to further administration of alkalies. The danger is also pointed out by this author, of pushing the reaction beyond that of the blood, for then albuminuria is liable to follow.

Fischer has always advocated the use of vegetables and fruits and, it now appears, with good reasons. Many of these foods are markedly efficient in producing less acid urine. That a food is a fruit or a vegetable, however, is no indication that the eating of it will decrease the acid formation. Thus, we have been able to show that prunes,

29. Fischer: Nephritis, New York, 1912.
30. Lewis, Ryffel, Wolf, Cotton and Barcroft: Heart, 1913, v, 45. Lewis, Ryffel, Wolf, Cotton, Evans and Barcroft: Proc. Physiol. Soc., Jour. Physiol., 1913, xlvi, 53.
31. Fischer, Martin H.: The Treatment of Nephritis and Allied Conditions, Jour. Am. Med. Assn., 1913, lx, 1682.
32. Palmer: Boston Med. and Surg. Jour., 1913, clxix, 464.

plums and cranberries cause an increased acid production rather than the expected decrease. This we have attributed to their content of benzoic acid. On the other hand, dietaries made up largely of potatoes with smaller amounts of apples, bananas, raisins and oranges offer an excellent means of introducing the desired bases into the body. These foods may all be obtained throughout the year and thus have a special advantage. A very suitable base-yielding food, which can only be had during the summer months, is the cantaloup. The tomato is also valuable. Care should always be taken not to eat too much of the cereals and meats, which have a predominance of acid-forming elements.

URIC ACID CALCULI

Uric acid concrements are estimated to comprise from 60 to 81 per cent. of all the varieties of urinary calculi. The formation of a given kind of calculus is, obviously, dependent on the reaction of the urine. A high urinary acidity favors the formation of uric acid calculi. Thus, Henderson[6] has shown that at the more acid reactions uric acid is present mostly in the free condition. As the H^+ decreases, more and more of the substance is in the form of urates. Our results show that acid urines are always supersaturated with uric acid and that they will experience precipitation when opportunity for the establishment of an equilibrium is given. On the other hand, alkaline urines are always capable of dissolving added uric acid, showing that as excreted they are not saturated. Kohler[28] has demonstrated that supersaturated solutions of uric acid experience spontaneous precipitation much more readily than do those of sodium urate. The correct prophylactic measures are therefore evident. In order to prevent a tendency to the formation of uric acid calculi, it is necessary that the urine be of low acidity and that the purin intake should not be too great. The first of these conditions can be fulfilled by the ingestion of alkalies and just as efficiently by eating some of the many suitable fruits and vegetables. These have a further advantage in that their purin content is negligible and therefore reduces to a minimum the exogenous output of uric acid. The value of such diets in the treatment of persons subject to uric acid calculi is also apparent.

SUMMARY

The composition of the urine is markedly influenced by the character of the food intake. Foods which have a preponderance of basic elements lead to the formation of a less acid urine. Conversely, foods with a predominance of acid-forming elements increase the urinary acidity. Potatoes, potato ash, oranges, raisins, apples, bananas and cantaloups are very efficient in reducing the acid output. Tomatoes are of less value in this respect. Rice and whole-wheat bread increase

urinary acidity. Plums, prunes and cranberries, although yielding a basic ash, nevertheless increase the acid formation. The latter foods contain benzoic acid, which increases the acidity owing to the formation of hippuric acid.

An increase in H^+ is accompanied by a significant increase in the ammonia excretion. Our results indicate that ammonia exerts an unmistakable influence in the preservation of body neutrality.

Titratable acidity and H^+ are closely related in behavior.

A lack of relationship between H^+ and urine volume is pointed out.

The solubility of uric acid in urine is closely dependent on the H^+. All urines with an acid reaction are supersaturated with uric acid, while alkaline urines are capable of dissolving added uric acid.

Further evidence for the interrelationship of the alveolar CO_2 tension and the H^+ of the urine is submitted and their dependence on diet is pointed out.

The H^+ of the urines of thirty vegetarians was 6.64, in contrast with the value of 5.98, reported by Henderson and Palmer, for persons living on a mixed diet.

I take pleasure in expressing my thanks to Prof. Lafayette B. Mendel for his kindly encouragement and advice during the progress of this and other work. I am also indebted to Prof. Harry W. Foote for the use of his solubility apparatus.

BOOK REVIEWS

A Practical Treatise on Medical Diagnosis for Students and Physicians. By John H. Musser, M.D., LL.D. Sixth edition, revised. Illustrated with 196 engravings and 27 colored plates. Lea and Febiger, Philadelphia and New York, 1913.

The sixth edition of Musser's "Diagnosis" is worthy of more than the usual perfunctory notice and congratulations. The gradual enlargement of the previous editions threatened the usefulness of the work. Condensation in such a case is obviously difficult, but this time it has been carried out with such excellent results that a long period of popularity seems assured. Although the text has been largely rewritten, it still retains the features that made it peculiarly valuable as a text-book and work of reference for physicians and students of medicine. It is full of the ripe knowledge of a keen observer and thoughtful and critical student, who combined with an unusual experience among all kinds of illness an enthusiastic love of collating, comparing and analyzing his own observations and those of others. In all the sections in which examination of patients is important, a wealth of information can be found. This should make the work especially valuable to beginners in clinical work, who may well turn to it as a commentary and guide to the puzzles and problems of the wards and out-patient department. The laboratory sections have been brought well up-to-date; their directions are clearly stated, and they also will be useful, though in many cases the student will need a more special handbook, as well as practice under a keen teacher in the preclinical work. Some comments on individual features are warranted. The section on "Diatheses" might with advantage be replaced with a new one in which the modern view of constitutions could be briefly set forth. Roentgenography is evidently getting to be too extensive to be included in a text-book on diagnosis, or if it is, must be handled by one who includes x-ray work in his daily activity. The relative value of the Widal test, that is, its lack of value as an early diagnostic factor, might have been more explicitly stated; there is still far too much reliance on it. The statement in regard to movable dulness in serofibrinous pleurisy seems to have come down from earlier days, and the description of the Grocco sign is correspondingly vague. Many of the additions to laboratory methods are inadequately indexed, but can be found if looked for. There seems need of a better test than the one given for chlorids in urine, however, now that that is of therapeutic value; also of more attention to nitrogen determinations, ammonia, urobilogen, diastase and oxybutyric acid. Blood viscosity would seem worthy of consideration. The statement in regard to embryocardia, page 274, that it is "heard in all conditions which cause a pronounced rapidity of the heart (over 120)," etc., is at least imperfectly expressed. The numerous illustrations are for the most part well chosen. That of Heberden's nodes represents a very remarkable condition and one we should like to know more about, but it does not give a correct idea of what Heberden and most writers after him had in mind. The diagram opposite page 704 gives a wrong impression of the enlarged veins in ascites with portal obstruction. The legends of the two taenia pictures, page 432, are transposed. These are but trifling defects in a work so full of accurate information as the new "Musser," and it may be confidently expected that within a short time the industrious author will more than make up for inevitable defects in a book dealing with so many and so diverse facts. Mechanically the work is well done.

BLOOD-PRESSURE IN MEDICINE AND SURGERY. A GUIDE FOR STUDENTS AND PRACTITIONERS. Edward H. Goodman, M.D.

At the present time there is no good book on blood-pressure in the English language. Yet the subject is one of vital and pressing interest. One looks with eagerness, therefore, on each new book, hoping that here at last one will find the essential combination of scholarship, clinical experience, and good judgment.

Unfortunately the latest work by Goodman is once more a disappointment. It is a conscientious, though far from complete, compilation of the literature on blood-pressure, but the material is not critically examined. Good, bad and indifferent, old and new articles receive almost equal consideration and (apparently) approval.

The author's own observations on the clinical side of the subject are good so far as they go, but are too few to add much to his summary of others' work.

On page 72 Féré is quoted as saying that attacks of cholera are dangerous to individuals suffering with disease of the arteries. Presumably "cholera" means choler, or anger. Similar slips are scattered through the book. Despite these limitations the book would be of use to any one who wishes to read a summary of a good deal that has been written on the subject of blood-pressure within the past fifteen years.